# The Journal of the International College of Surgeons

Official monthly publication of the International College of Surgeons

CONTENTS

VOLUME 29, NUMBER 1
JANUARY, 1958

**GENERAL SURGERY**

Models and Moulages: Their Use in Teaching ..... 1

*Mark M. Marks, M.D., F.I.C.S., D.A.B., Kansas City, Missouri*

Ambulatory Injection Repair of Inguinal Hernias ..... 8

*Frank H. Baehr, M.D., Ph.B., F.I.C.S., Springfield, Massachusetts*

**GENITOURINARY SURGERY**

Tumors of the Renal Pelvis and Ureter ..... 22

*Theodore R. Fetter, M.D., F.A.C.S., D.A.B., and J. Louis Wilkerson, M.D., Philadelphia, Pennsylvania*

The Variant Renal and Suprarenal Blood Supply, with Data in the Inferior Phrenic, Ureteral and Gonadal Arteries: A Statistical Analysis Based on 185 Dissections, with a Review of the Literature ..... 41

*Robert J. Merklin, Ph.D., and Nicholas A. Michels, Dr. Sc., F.I.C.S. (Anat.), Philadelphia, Pennsylvania*

**NEUROLOGIC SURGERY**

Use of Radioactive Colloidal Chromic Phosphate for Prevention of Amputation Neuroma ..... 77

*John I. Perl, M.D., F.A.C.S., Chicago, Illinois, and David G. Whitlock, M.D., Syracuse, New York*

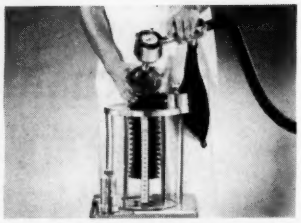
**OBSTETRIC AND GYNECOLOGIC SURGERY**

The Pathologist's Approach to Preclinical Carcinoma of the Uterine Cervix, with Special Reference to Diagnosis and Management ..... 92

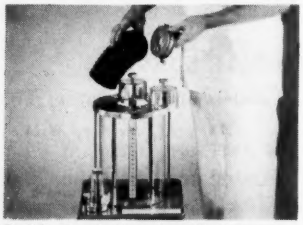
*Edward H. Soule, M.D., Rochester, Minnesota*

# New features of the Jefferson Ventilator

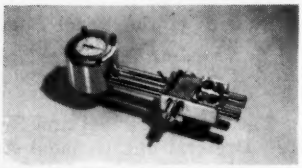
**New Volume-Indicator model GH-3** makes possible a more precise estimate of tidal exchange, while automatically delivering independently adjustable negative and positive pressures at desired rate and phase to provide proper pulmonary ventilation.



**Vertical scale shows delivered volume,** and convenient chart on platform gives corrections for gas flow at various rates of respiration (essential for accuracy with any bellows-type volume indicator).



**Simplicity of construction and operation** is characteristic of the JEFFERSON VENTILATOR. Trouble-free, automatic overflow valve in collar casting prevents overfilling bellows during high gas flows.



**New, optional NRB Head,** for use with any model JEFFERSON VENTILATOR, for the first time makes possible mechanical ventilation with intermittent negative and positive pressures during non-rebreathing anesthesia techniques.

THE JEFFERSON VENTILATOR is a clinically proved, auto-pneumatic, portable device to help insure proper pulmonary ventilation during general anesthesia in every type of patient, and especially in the poor-risk patient or during open-chest surgery. Separate controls for phase, rate, negative and positive pressures maintain optimal mean airway pressure. Simply designed and easily regulated, the JEFFERSON VENTILATOR is now used routinely in the teaching hospitals of more than three-quarters of medical schools throughout the United States.

AUTOMATICALLY delivering properly phased negative and positive pressures through the endotracheal tube, the JEFFERSON VENTILATOR helps prevent respiratory acidosis, does not embarrass circulation, frees both hands of the anesthesiologist. However, manual control of rebreathing bag may be quickly resorted to if desired. Finally, negative and positive pressures, rate and phase of the JEFFERSON VENTILATOR may be adjusted *separately* to changing requirements. *For orders or information, phone collect:* OSborne 5-5200, AIR-SHIELDS, INC., Hatboro, Pa.

**The Jefferson Ventilator***

*Manufactured, sold & serviced by* **AIR-SHIELDS, INC.**

*Trademark

**ORTHOPEDIC SURGERY**

Simple Laminectomy for Spondylolisthesis, Without Spinal Fusion.....101
*Robert Dean Woolsey, M.D., F.A.C.S., St. Louis, Missouri*

Pollicization of the Index Finger: Report of a Case.....106
*Timothy A. Lamphier, M.D., F.A.C.S., F.I.C.S., D.A.B., and Malvin F. White, M.D., D.M.D., Boston, Massachusetts*

**SURGERY OF THE THYROID AND PARATHYROIDS**

Hyperparathyroidism .....113
*Irving L. Lichtenstein, M.D., F.A.C.S., F.I.C.S., D.A.B., and Marvin S. Levy, M.D., F.A.C.P., D.A.B., Beverly Hills, California*

EDITORIAL

The Application of Cardiopulmonary Physiology .....126
*Maurice G. Buckles, M.D., and Mostafa Daneshvari, M.D., Columbus, Ohio*

NEW BOOKS .....128

ABSTRACTS FROM CURRENT LITERATURE.....131

## ARTICLES TO BE PUBLISHED

The Lymph Nodes in the Mediastinum
*Ernst Beck, M.D., F.A.C.S., and E. J. Beattie Jr., M.D., Chicago, Illinois*

Total Gastrectomy for Carcinoma
*I. Boerema, M.D., F.I.C.S. (Hon.), Amsterdam, The Netherlands*

Experimental Use of Lugol's Solution and Starch as a Test for Pregnancy
*Nicholas Minischia, M.D., A.I.C.S., Cleveland, Ohio*

Ureterovaginal Fistulas
*Alexander Slavcoff, F.A.C.S., D.A.B., Harrisburg, Pennsylvania*

# Before and after surgery

*effective for anxiety, tension and insomnia*

- reduces preoperative fear
- helps ensure natural sleep without morning hang-over
- no significant lowering of blood pressure
- no respiratory depression
- well tolerated, relatively nontoxic

# Miltown®

THE ORIGINAL MEPROBAMATE
DISCOVERED & INTRODUCED BY
WALLACE LABORATORIES
NEW BRUNSWICK, NEW JERSEY


**REFERENCES:**

1. *Rushia, E. L.: Preliminary report on the use of meprobamate for pre-anesthetic sedation. J.M.A. Georgia* **46**:*93, March 1957.*
2. *Lamphier, T. A.: The role of meprobamate in postoperative surgical care. Ann. New York Acad. Sc.* **67**:*810, May 9, 1957.*
3. *Kern, E. C.: Preoperative sedation with meprobamate (Miltown) in surgery of eye, ear, nose and throat. Eye, Ear, Nose & Throat Month.* **36**: *408 July 1957.*


CM-6086

FOUNDED BY DR. MAX THOREK

# The Journal of the International College of Surgeons

FOUNDED IN GENEVA, SWITZERLAND, 1935 - INCORPORATED IN WASHINGTON, D. C., 1940

Vol. 29 JANUARY, 1958 No. 1

## General Surgery

# Models and Moulages: Their Use in Teaching

MARK M. MARKS, M.D., F.I.C.S., D.A.B.

KANSAS CITY, MISSOURI

RECENT advances in the development of synthetic materials with plastic properties have stimulated interest in model making. In the past, models used in medical teaching have been constructed of wax, papier mache or plaster of paris. Those produced in quantities by mass production methods were often poorly done. The better ones required a high degree of artistic skill and much time to produce; this made them expensive and rare. Some were subject to deterioration from aging and changes in temperature. Others, because of their fragility, were usually relegated to a glass case for observation and became unavailable for close examination.

For these reasons, models have not been adequately employed in basic science classes or in medical schools. Good models can be particularly helpful in such subjects as embryology and comparative anatomy. Microscopic objects enlarged in models will show greater detail. Models can be of inestimable value in the study of anatomy, as exhibits to illustrate special operative measures, and in the recording of actual surgical observations at operation or at autopsy. Other subject matter for model and moulage making can be obtained from a variety of sources, e.g., one's own knowledge or drawings or photographs in medical texts.

It is my purpose in this paper to describe relatively simple methods for making models and moulages that are particularly suitable for medical teaching. They

From the Section of Proctology, Department of Surgery, Menorah Medical Center, Kansas City, Missouri.
Submitted for publication Oct. 24, 1957.

Fig. 1.—Freehand drawing on plyboard.

are made of readily available materials, require little skill to make, and can be handled without fear of breakage. Their accuracy is good and their cost small.

Five basic steps are required in making these models: (a) drawing, (b) modeling, (c) making the mold, (d) pouring the positive solution and (e) coloring. The form to be fashioned is first drawn with a pencil on a piece of thin plywood 4 inches (10 cm.) larger than the form itself. Enlargements of drawings from other sources are made by multiplying the size of squares. If the original drawing is lined with half-inch squares, the plywood is covered with 1 inch squares to double the dimension or multiples of ½ inch for the desired increase. A freehand drawing is usually sufficient, since the penciled lines are used only as a guide (Fig. 1). When the sketch is completed, plastiline or oil clay is placed to conform to the drawn figure and roughly shaped to make a bas relief (Fig. 2). The use of a sculpturing tool defines detailed formations more clearly; care should be taken not to create overhanging clay or lipping that could interfere with removal of the cast.

Investment material may be plaster of paris, ceramic plaster or commercial molding plaster such as is used in construction work. To make liquid plaster for taking impressions, a quantity of water estimated to cover the clay to a depth of ½ inch is first put into a mixing bowl. Dry plaster is rapidly sprinkled into the water until the latter will absorb no more fluid. Not until then should the mixture be stirred by hand or with a spatula until it is smooth. To remove air bubbles that may interfere with reproduction, the container with the liquid plaster should be gently bounced. When the plaster begins to thicken slightly, it is slowly poured over the modeled clay until the latter is evenly and completely covered. If the piece is larger than a foot square, gauze or cheesecloth incorporated into the mold at this stage will strengthen it and prevent breaking. Should weak or thin spots in the mold become apparent or be suspected, more plaster and water can be mixed and added to make the entire cast ½ to ¾ inch thick.

When the cast becomes warm, it has hardened sufficiently to be safely moved for separation from the clay. Depressing the edges of the plywood board away from the plaster will loosen the cast so that it can be lifted free from the clay model. If separation is difficult and some clay adheres to the plaster, it can be removed with a wooden applicator stick. This will prevent damage to the negative and interference with good reproduction. While the plaster is still moist, additional carving with a sharp tool may be done if required. The plaster negative is dried at room temperature (Fig. 3). If a quick drying is desired, it may be slowly warmed in an oven.

The positive solution consists of three parts, clay, water and latex. The last-mentioned substance is a synthetic, water-soluble rubber. The purpose of this mixture is to make a rubber-based slip or thick liquid which, when put into a dry plaster mold that extracts the water, builds up a clay-rubber layer giving the exact impression of a positive form. The proportions of the component parts of the positive solution are water, 25 per cent; McNamara clay, 25 per cent, and anode latex, 50 per cent. The clay is water-washed and is high in kaolin, and is made up of exceedingly fine particles. The water and clay are mixed before being added to the latex. In this combination the ingredients form a thick, viscous liquid. The solution may be obtained in this formula from the Latex Corporation of Chicago or may be purchased separately from ceramic or chemical establishments. If the mixture is produced by the model maker, 20 drops of sodium silicate added to 1 pint of the latex-clay mixture will act as a deflocculent and keep it from separating.

The plaster mold should be bone-dry before it is used. To make the positive impression it is best to level it and make it secure to receive the liquid. Care must be exercised to prevent spillage, because of the latex-clay mixture's adherent properties in the fluid state. The cavity of the plaster negative is filled slowly to prevent air pocketing and splashing. When full to capacity, the cast is left undisturbed for thirty to forty minutes or until a clay-latex wall 1/8 inch thick has accumulated. The remaining liquid is returned to air-tight container and stored in a cool place for future use.

Impressions made in this way need backing to stiffen them and help maintain their shape. To do this the remaining portion of the cavity in the mold is filled with crumpled paper, gauze or mechanic's cotton waste. Some of the positive solution can be used as a binding material to anchor the backing to the impression itself for greater stability. The completed form is set aside at room temperature for twenty-four to seventy-two hours, depending upon

Fig. 2.—*Above*, clay model ready for casting. *Below*, model of section through female pelvis in knee-chest position.

the size. This allows for air-curing of the clay-latex in the cast. After the model has been removed from the mold, it is dried again for another twelve hours. There will be about 5 per cent shrinkage. The form is then ready for coloring. I find that pigments in casein and in acrylic polymers in latex give the models a more realistic coloration. Both may be obtained in an art shop. The advantage of these over other types of colors is that they are permanent, dry rapidly and remain flexible for longer usage. The accuracy of coloration is dependent upon the care and diligence of the model maker (Fig. 4).

Moulages are molds or casts taken directly from a portion of the body. Such impressions obviate the need for modeling. Face masks or impressions of skin lesions are examples of this. When this procedure is combined with sculpturing in plastiline, however, many possibilities become evident.

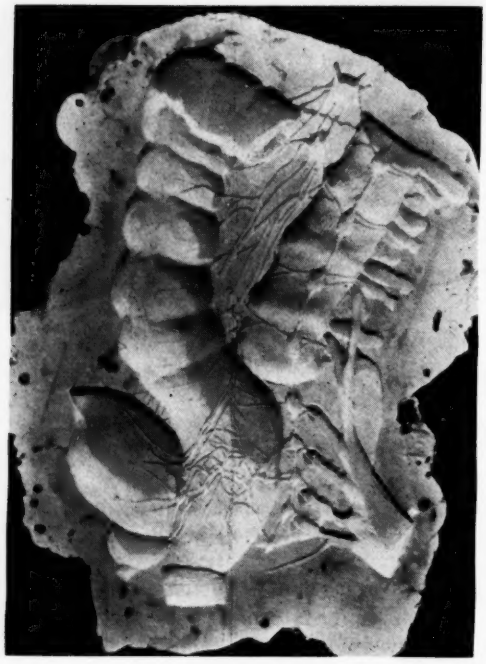


Fig. 3.—Plaster cast of clay model.

When a body surface impression is taken, the cavity, or negative, in the plaster can be carefully packed with clay to return the original surface. By dissecting the clay and modeling the structures beneath, the anatomic character of the parts can be demonstrated. As further plaster impressions are made of the sculptured parts of the dissection, a series of moulage-models can be easily produced to show structures at various levels.

To illustrate such a project, suppose a thyroidectomy is to be shown. A plaster impression is taken of the neck and upper part of the cadaver. When the plaster hardens it is removed. Clay is carefully pressed into the cavity to pick up skin texture and body shape. When the plaster is removed, the clay, simulating the original form, is ready for modeling. The line of incision is made in the clay as it would be in the skin. A plaster impression is made of it, along with the surrounding area. As the skin flaps are raised and other structures normally encountered are modeled, impressions are taken at each important step and removed until the series is complete. When all of the plaster casts are dry, the cavities are filled with the positive solution and the moulages finished as previously described. To simulate naturalness still further, the dissected parts are painted with a clear plastic glaze after coloration, to heighten the colors and produce highlights that give the illusion of moisture.

The same procedure can be followed to portray and illustrate such things as axillary, perineal, neck, and other dissections; the Glover operation for coronary artery disease; displaced intravertebral discs; hernias; amputations; plastic or orthopedic procedures and, for that matter, nearly all operations that can be doc-

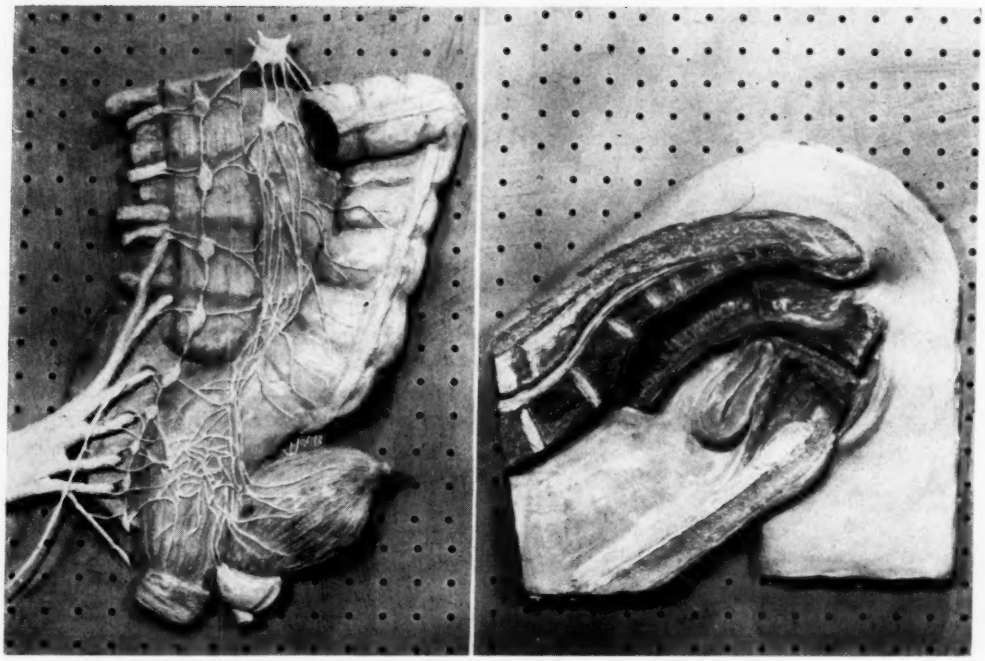


Fig. 4.—Models completed, showing innervation of left half of colon and female figure.

umented for teaching, reference or permanent record.

Bones can be accurately reproduced by casting them in multiple piece molds and using a synthetic resin in a liquid state that hardens into a horny material when dry (Fig. 6). Other synthetic resins, such as styrene chloride, are suitable for smaller model and moulage making. This and other like substances require maturing at 375 F. for fifteen minutes in metal molds.

Another potentiality of model and moulage making that should be explored is what it can do for the student. It has been shown that those who learn the process through a specific project of their own gain much more from the subject. The better specimens made by these students can be used to teach following classes. Most students, through this experience, find a new medium for their training.

I have found these models useful in my office practice, for in my experience most patients are vitally interested in the nature of their ailments and not only are grateful but become more cooperative when the physician takes them into his confidence. In many instances a careful explanation with such an illustration removes much of the unnecessary mystery and establishes greater confidence. Models and moulages such as I have described have been employed for this purpose with good effect.

On television and in medical motion pictures models and moulages of this type have been extremely useful, because of their realism, in illustrating special anatomic problems and orienting surgical procedures.

Fig. 5.—Sagittal section through anterior rectal wall, prostate and bladder.

Fig. 6.—Reproduction of pelvis.

## CONCLUSION

Because of the magnitude of medical teaching, any means that can accelerate the student's learning is worth while. Previous methods for making useful three-dimensional models and moulages have seemed formidable to those who could use them for instruction. A method of making such models and moulages is described that affords access to endless possibilities as new materials are developed. Their uses are explained in detail.


## RÉSUMÉ

Etant donné le domaine très vaste des études médicales, tous les moyens susceptibles de les faciliter et de les accélérer doivent être pris en considération. Certaines méthodes permettant de fabriquer des modèles et moulages à trois dimensions ont été accueillies avec enthousiasme par les professeurs. L'auteur décrit une méthode inédite donnant des possibilités infinies grâces à des matières nouvelles.

## CONCLUSAO

Devido a magnitude e importancia do ensino médico qualquer meio de treinamento dos estudantes deve ser considerado importante. Os métodos anteriores utilisando modelos e modelagens tridimensionaistem sido formidaveis para os que os utilisam como elementos de ensino. O A. descreve a técnica de faser esses modelos e modelagens, usando recursos para utilisar ao máximo as possibilidades dos novos materiais. Explica o uso pormenorisadamente.

## SCHLUSSFOLGERUNGEN

Angesichts des Umfanges des Materials des medizinischen Unterrichts ist jedes Mittel, das dem Studenten ein schnelleres Lernen ermöglicht, zu begrüssen. Frühere Methoden der Herstellung nützlicher dreidimensionaler Modelle und Moulagen scheinen die Lehrer, die solche Hilfsmittel gebraucht hätten, von ihrer Anwendung abgeschreckt zu haben. Es wird ein Ver-

fahren zur Anfertigung solcher Modelle und Moulagen beschrieben, das infolge der Entwicklung neuer Materialien unabsehbare Möglichkeiten eröffnet. Ihre Anwendung wird im einzelnen dargestellt.

CONCLUSIONI

La vastità dell'insegmento medico rende degno di considerazione ogni mezzo che consenta di affrettare la preparazione degli studenti di medicina. L'impiego, ad esempio, di calchi e modelli a tre dimesioni si è dimostrato di incalcolabile utilità.

L'autore descrive appunto un metodo per costruire tali modelli e per usarli con profitto.


## IMPORTANT NOTICE TO ALL PARTICIPANTS IN CONGRESSES AND REGIONAL MEETINGS OF THE INTERNATIONAL COLLEGE OF SURGEONS

Those desiring their Congress presentations to appear later as articles in the **Journal of the International College of Surgeons,** please note:

1. **A full copy of the manuscript, together with all illustrations, legends, tabular matter and bibliographic references,** should be sent DIRECT to the Editorial Office, Journal of the International College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Illinois. Manuscripts so submitted will be promptly acknowledged and, on acceptance by the Editorial Board, published as soon after the Congress as possible. The Journal **cannot be held responsible for loss, failure of acknowledgment, delay in publication or nonpublication of any manuscript, or any subsidiary material appertaining thereto, which has not been submitted through the official editorial channels.**

2. Manuscripts may be submitted in advance of the Congress if desired. When this is done, they should be **plainly marked with the name, place and date of the Congress or Meeting concerned,** to guard against premature publication.

3. Manuscripts delivered in person to Congress officials or others **for press reportorial use only** should be sent by the recipient to the Public Relations Bureau.

4. If illustrations are desired and it is impossible to submit them at the time the manuscript is submitted, the notation "Illustrations to come" should accompany the latter; otherwise the article may be scheduled for publication before the illustrations have arrived.

These requests are made not only to safeguard the Journal from error but in the best interests of our contributors. To make sure of prompt acknowledgment and efficient handling of your Congress presentation, please send it DIRECT to its ultimate destination!

# The Ambulatory Injection Repair of Inguinal Hernias

FRANK H. BAEHR, M.D., Ph.B., F.I.C.S.*

SPRINGFIELD, MASSACHUSETTS

AN ambulatory injection treatment for male inguinal hernias that produces, by piezoelectricity, a nonabsorbent granulomatous tissue that acts as a permanent internal truss beneath the external oblique aponeurosis of the groin will be described. This procedure is based upon twenty years' practical experience in selected cases. An evaluation of the end results of all inguinal hernias treated in a three-year period with an eight- to ten-year follow-up shows that the technic described overcomes the problems encountered with earlier methods. In order to obtain statistical information on which to base a conclusion with respect to results, 214 male patients with 261 inguinal hernias treated in the office, with the treatment completed during the years 1946, 1947 and 1948, were followed up from September 1955 to September 1956.

Experience has shown that two factors are essential to success with the ambulatory treatment: (1) a sclerosing solution that produces a nonabsorbent tissue in the affected area of the groin, and (2) a reliable truss to support the patient completely and without discomfort throughout the treatment.

The means of evaluating results, experiences, observations and the underlying causes of failure will be discussed.

*History of the Injection Treatment.*—As far back as 1880, so noted a surgeon as Billroth[1] stated that radical operation for hernias could be done away with if artificial proliferation of tissues could be produced. About 1900, Mayer[2] of Detroit modernized the ambulatory treatment originated by Velpeau[3] in 1835. During the 1930's Bratrud and others[4] reported excellent initial results with the injection treatment in large series of cases. Biopsies performed by Kelly[5] on injected animals at ten-day intervals, however, showed that early fibroplastic tissue had practically disappeared in one hundred days and had been largely absorbed within fifty days. Dobson,[5] in 1940, confirmed Kelly's experiments. Coley,[5] of the Hospital for the Ruptured and Crippled in New York City, observed 81 per cent of relapses after injection treatments. At this time the Council of the American Medical Association, in its official Journal,[6] stated: "After due consideration of a second hospital survey the Council reaffirms its previous opinion that the Injection Treatment may not be recognized for general use. Universal employment of the method is to be deplored." Since that period there has been a dearth of scientific articles on this subject.

In 1949, however, Koontz[7] stated, "The injection method has a place in the treatment of hernia, especially for patients coming in the following categories: (a) elderly persons unsuitable for operation due to the infirmities of old age; (b) persons rejected for industrial employment because of enlarged rings, with doubtfully demonstrable hernias; (c) patients who will not or cannot be operated on for personal reasons; (d) persons with certain types of recurrent hernias with small fascial defects." To this may be added pa-

*Former Visiting Surgeon, State Cancer Hospital, Westfield, Massachusetts; Consulting Surgeon, Health Department Hospital, Springfield.

Submitted for publication Aug. 31, 1957.

tients who, for any reason, cannot absent themselves from their jobs for any length of time.

*The Sclerosing Solution.*—Several different mixtures of irritating chemicals, manufactured by well-known pharmaceutical concerns, were tried prior to 1944. These irritating chemicals produced fibrous tissue when introduced into the inguinal canal, but the areas of injection had to be well overbuilt to allow for natural resorption of the irritant, which often occurred after the procedure had been completed. This resorption varied in amount in different patients, but seemed greatest in men over 50 years of age. Often the patients so treated would require extra injections after their original series had been completed, in order to prevent a recurrence. No doubt this resorption, with consequent opening of the canal, was the main reason why many surgeons discontinued the ambulant injection treatment. It became evident that a new sclerosing solution was needed to form a permanent tissue.

A search through the medical literature disclosed the discovery made by McNally and Bergman[8] during their investigation of silicosis in 1935. These two men abandoned the theory that the hardness and sharpness of silicon particles alone produced the chronic pathologic conditions and strange fibrous tissue associated with silicosis of the lungs. They decided that silicosis is caused by the action of the blood fluorides on the silicon molecule, forming soluble tetrafluoride and thus producing fibrotic changes. The theory that fibrosis of the lungs is caused by the chemical action of sodium fluoride in the blood upon silicon dioxide was novel. To test it out, these investigators made up a near-colloidal solution of calcium fluoride containing finely suspended particles of silicon dioxide or quartz and injected it into animals. These injections produced non-absorbent fibroplastic tissue similar to that observed in cases of silicosis. This discovery prompted McNally and Bergman[8] to advocate the use of such a solution for the injection treatment of inguinal hernias. The solution was called Alparene No. 2.*

*The Piezoelectric Theory.*—Evans[9] in 1948 and Evans and Zeit[10] in 1949 demonstrated that when silicon dioxide (quartz) is deposited in living tissues a fibroplastic effect is produced. The silicon dioxide (quartz) crystals belong to a class that lacks a central point of symmetry; they are therefore piezoelectric. These authors defined "piezoelectric" as that property of asymmetric crystals that causes them to develop electrical charges when compressed or overextended in particular directions. Cough, strain, muscular activity, arterial pulsation or any physiologic mechanism that can bring about a squeezing of the piezoelectric crystals deposited in the tissues is capable of producing a current of electricity. Kaplan[11] in 1953, added mechanical pressure from restricting garments and trusses. These asymmetric crystals are observed to be fibrogenic when introduced as a finely divided dust into living tissue, uniformly producing proliferative fibrous reactions. Evans and Zeit[10] postulated that crystalline materials are fibroplastic if they are relatively insoluble in body fluids, are in the asymmetric (piezoelectric) crystal group, and are electrically nonconductive, of a proper particle size and in sufficient particle concentration. Alparene No. 2 is in this class.

In 1953, Kaplan[11] removed nodular masses that had been formed after Alparene No. 2 had been injected into the groins of 4 patients who had been treated by the ambulant method.

Examination revealed that the reaction of tissue to silaceous material appeared to be primarily fibroplastic, with little or no inflammatory response. Investigations to

*Dequin Physicians Products Co., Chicago.

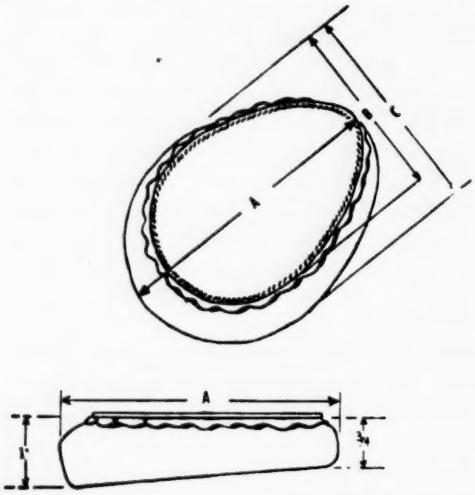



Fig. 1.—Inguinal pad. In upper drawing line *A* is 4 inches (10 cm.) in actual length; line *B* is 2½ inches (6.2 cm.) long, and line *C* measures 3 inches (7.5 cm.). Lower drawing (view showing depth of pad) repeats line *A*. Pad is 1 inch (2.5 cm.) thick at lower end (shown on left) and ¾ inch (1.9 cm.) thick at upper end (shown on right).

determine the factors responsible for this type of tissue response revealed early that the concentration of silica and its particle size determined the development of the nodular fibrosis characteristic of this material.

On the basis of the work of Evans and Zeit[10] and Kaplan[11] one may assume that it is the piezoelectric process which causes the pronounced fibrogenesis.

*Support During Treatment.*—Two trusses are required to be worn by the patient: (1) a semirigid truss for day wear and (2) an elastic one to be worn in bed. The semirigid truss keeps an even support of the groin, even under pressure. The framework of the semirigid truss encircles two thirds of the body, and elastic webbing encircles the other third. An ovoid inguinal pad (Fig. 1), thicker at the medial end than the lateral, and entirely covering the involved groin, is applied just lateral to the base of the penis. The covering of the external ring and the lateral part of the pubic bone is most essential, as the first four to six injection treatments completely close the external ring and apparently fuse this area with the pubic bone. A perineal leg strap without any tension is added to the framework (Fig. 2).

The truss made entirely of elastic webbing, with the same type of ovoid inguinal pad, is used for bed wear. (The construction and application of these trusses will be discussed in a later article.)

*Selection of Patients.*—Male patients who can be successfully treated are those with small to medium sized inguinal hernias, either direct or indirect or a combination of both, with good musculature that can be comfortably and completely held at all times by a properly fitted truss, and in whom the external ring is not greater than 3 cm. in diameter.[12]

The exceptions are patients who have a coexisting chronic cough, are obese, have large varicoceles, or have severe constipation or urinary obstruction caused by a hypertrophic prostate. The injection therapy has not been successful for women, owing to anatomic differences.

*The Role of the Patient.*—The patient must be conscientious and cooperative to insure maximum success with the injection procedure. He must wear the semirigid day truss while up and about and the elastic night truss with the same type of

*Recurrent Hernias*

| No. of Patients | No. of Hernias | Recurrences within 2 Years | Recurrences from 2-10 Years | Total Recurrences |
|---|---|---|---|---|
| 205 | 249 | 13.7%<br>34 cases | 10.8%<br>27 cases | 24.5%<br>61 cases |

elongated ovoid pad while in bed. The night truss must be worn for two months during the initial part of the treatment. As a precautionary measure during this period, the patient must change from his day to his night truss while lying on his back. No tub baths are allowed until after the first four to six injection treatments. At the end of this period (four to six weeks) the external ring should be completely and tightly closed and the patient may take tub baths without support. Prior to this time, sponge or shower baths are prescribed and are taken in the morning with the night truss on. After the bath the elastic truss is wrung out and hung up to dry in readiness for wear again that evening.

*Office Requirements.*—The following equipment is needed for office treatment:

1. A sterile short beveled 3 inch No. 18 bore needle attached to a 5 cc. Luer-Lok syringe

2. Gauze pads and alcohol

3. A wide-mouthed bottle of oil of sesame with 3 per cent phenol

4. A 60 cc. rubber-capped vial of Alparene No. 2. (Alparene No. 2 consists of calcium fluoride and silicon dioxide in the form of a "near colloidal" suspension containing 2.5 Gm. of each per 30 cubic centimeters of solution.)

*Treatments and Doses Required.*—The reactions to Alparene No. 2 vary with the individual patient. With experience, I have learned that the dosage can be kept at a level at which minimal soreness and swelling are involved.

The average patient may or may not have some soreness and swelling after the first three or four injections. If he does, it usually is not severe enough to keep him from carrying out his daily routine.

The suggested doses are:

First treatment: 1 cc. of Alparene No. 2 diluted and mixed well with 3 cc. of oil of sesame with 3 per cent phenol

Second treatment: 2 cc. of Alparene No. 2 with 3 cc. of oil of sesame with 3 per cent phenol

Third treatment: 1 cc. of Alparene No. 2

Fourth treatment: 2 cc. of Alparene No. 2

Fifth to tenth treatments: Usually 2 cc. of Alparene No. 2, given once or twice weekly if no soreness exists

Subsequent treatments: 2 cc. of Alparene No. 2.

For very muscular patients, doses beyond the tenth may consist of 3 cc. of Alparene No. 2. Very thin patients usually require a lesser number of treatments and smaller doses.

To the average well-developed male patient the first four to six injections are given at weekly intervals. Each one is made just inferior in position to the preceding one, taking in the width of the inguinal canal. Some patients who have complained of a "dragged-down feeling" find that this disappears after three to four injections. As a rule, these four to six injections completely close the external ring, and no protrusions or impulses can be felt when the patient coughs or strains. Closing the external and internal rings tightly does not permanently interfere with the blood supply of the testes. The medial third of the canal will now be quite solid and will seem fused to the pubic bone, and Hesselbach's triangle will be reinforced, which can prevent thinning out of this area in middle life. This apparent localizing of the solution in the medial third of the canal is probably due to man's upright position, which forces more of the chemical to be deposited near the pubic bone and therefore causes hardness in this area first. Subsequent injections, averaging ten to fifteen more, are made in the same pattern, but usually only in the lateral two-thirds of the canal and posterior to the newly formed tissue. Invagination of the scrotum with the left index finger is done prior to these injections only to determine the location of the closed external ring, which aids in determining the direction of the needle. Palpation of the injected areas of injection may reveal small spots that are

not uniform in thickness. Experience will show that if one places small amounts of the chemical beneath the fascia and into these areas, granulomatous tissue growth can be placed where needed and to the amount required. There will be a coalescence or fusion of the different areas of nodular fibrosis, eventually forming one solid mass or pad.

It can be concluded, therefore, that the pronounced fibrosis tends to close the defects in the transversalis fascia, tighten the hernial rings, close off the sac and unite into one piece the external oblique aponeurosis, the internal oblique and the transversalis muscle and fascia, leaving only a narrow passageway for the spermatic cord in the reconstructed inguinal canal.

The ambulant method of treating inguinal hernias may vary with different surgeons, as does the surgical technic for hernia repair. Twenty years' experience, however, has taught me that in order to get the most satisfactory results all hernias accepted for this procedure should be treated as direct indirect hernias, with the exception of some of the surgically recurrent hernias. These will be discussed in the paragraphs on technic.

*Technic; Subfascial Fulcrum Test.*—The patient first lies horizontally on the examining table. If the table breaks on one end, he may flex his knees at right angles and rest his feet on a step. The Trendelenburg position is rarely used, and the patient must have his arms at his side.

The truss is always examined before and after the patient receives his treatment and is adjusted if necessary. The pubic hair is not shaved off or clipped. The leg strap is then released from its attachment to the pad, and if the pad should then follow the receding surface of the abdominal wall the trussmaker should bend the framework to correct this. The pad is then pulled upward to rest on the upper part of

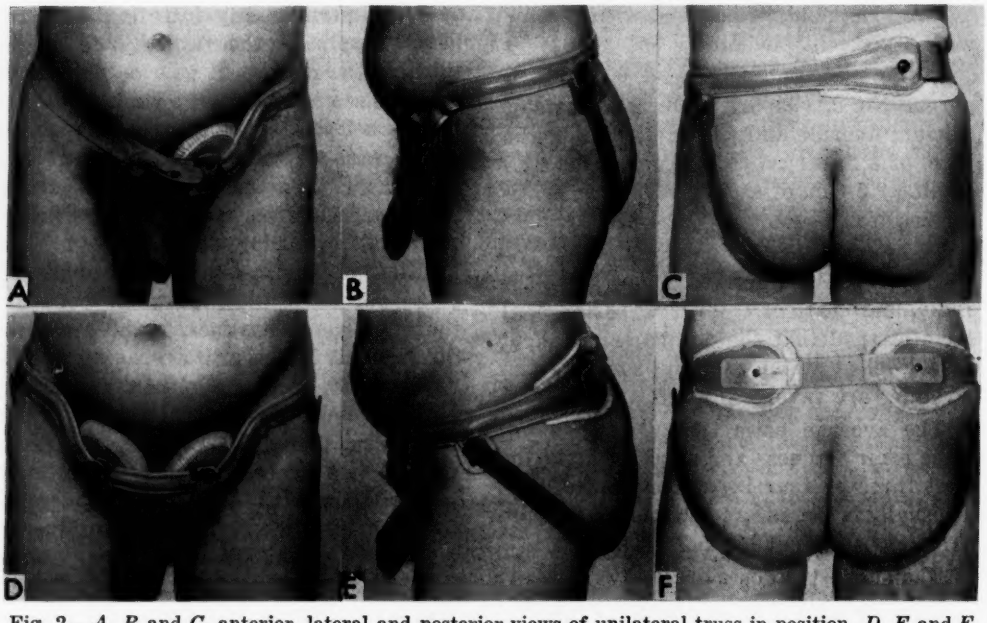



Fig. 2.—*A*, *B* and *C*, anterior, lateral and posterior views of unilateral truss in position. *D*, *E* and *F*, same view of bilateral truss.

the abdomen, and the groin is inspected to make sure that the hernial contents have been fully reduced into the abdomen. The sac itself is almost never reduced, but when the sac is completely empty its walls will be in direct contact with each other. The internal inguinal ring is next located. This, in the case of a left inguinal hernia, is done by the surgeon's putting his left thumb on the pubic spine and his middle finger at a point 1 cm. above the middle of Poupart's ligament and about ½ cm. medialward. The groin to be treated by injection is well cleansed with an alcohol sponge.

There is a "feel" or "give feeling" when the 3-inch No 18 bore needle punctures the external oblique fascia, similar to the "feel" one gets when the needle goes through the dura in a spinal puncture. Rice[12] has described a subfascial fulcrum test that allows one to know what instant the needle passes through this fascia and exactly where the needle point is. He stated, "After the needle has passed through the skin and subcutaneous tissue, the needle point can be palpated by depressing the syringe and elevating the point, with the skin as the fulcrum. Knowing then that the needle has not passed thru the fascia, it is held lightly and very gently pushed upon. As the needle passes through the fascia, it encounters a slight resistance. If the pressure is continued steadily but lightly, it will soon give way when it suddenly passes thru the fascia. If the needle point is now elevated, using the skin as the fulcrum, its point cannot be palpated. This simple test determines the position of the needle point under the fascia and is probably the most important factor in determining the correct position of the injection." During the past few years this test has been done before withdrawal of the needle with the empty syringe attached, so as to ascertain whether or not all of the solution has been deposited beneath the fascia. If some of the chemical is deposited anterior to this fascia in the subcutaneous fat, nodules and granules of granulomatous tissue will be formed, which will adhere to the external oblique aponeurosis. This will eventually cause a hard swelling to develop and produce permanent bulging of the inguinal region.

With the location of the left internal ring, the surgeon next invaginates the scrotum with the tip of his left index finger just under the base of the penis and, going lateralward, locates the external ring. At a 45-degree angle, the needle then punctures the skin and subcutaneous tissue at the superior part of the internal ring, going through the aponeurosis of the external oblique and the conjoined tendon and entering the inguinal canal. In the same direction as the obliquity of the canal, it is gently pushed down to the invaginated tip of the left index finger at the upper part of the external ring. After aspiration to make sure that no blood vessel has been entered, the needle is slowly withdrawn, while slight pressure is put upon the exposed end of the plunger of the syringe, making sure that the chemical is pooled. As the needle point reaches the internal ring and the solution has been deposited along the entire length of the canal, the subfascial fulcrum test is made and then the needle is entirely withdrawn from the groin. If this is properly done, there should be no localized pain or burning. If pain is elicited, however, one should withdraw the needle slightly and reroute it. The pad is then reapplied to the groin, the leg strap attached to the pad and the patient allowed to get up from the table.

For the newcomer in this field it may be helpful to dip the tip of the needle in gentian violet or methylene blue for the first few injections, so that the dye will leave a mark. This makes it easier to determine the location of subsequent injections.

*Technic for Recurrent Surgical Hernias.*—The majority of surgically recurrent inguinal hernias become direct hernias. Observation and experience have shown that some so-called recurrent surgical hernias are nothing more than concomitant direct inguinal hernias that were overlooked during the primary operation. These recurrent hernias are treated by injecting the canal, particularly the lower third or the lower half. Surgically recurrent inguinal hernias, consisting of small localized fascial holes that are usually due to a suture cutting through the tissues or to a localized infection, are treated by depositing the chemical, without pooling, beneath the external oblique fascia into these areas. The granulomatous tissue then fills in the defects. Usually fewer treatments are used for this type of inguinal hernia.

*Technic for Potential Hernias*: The potential inguinal hernia, always an industrial problem, can be permanently relieved and the enlarged rings completely closed with a few injections. The patient will then be free from impulses and acceptable for employment.

*Group Studies.*—The original diagnoses in the cases of 214 patients aged 15 to 79, with 261 inguinal hernias (47 being bilateral), were as follows:

| | |
|---|---|
| Right indirect | 18 |
| Left indirect | 14 |
| Right direct indirect | 97 |
| Left direct indirect | 85 |
| Left indirect scrotal | 3 |
| Left direct indirect scrotal | 1 |
| Right recurrent surgical | 13 |
| Left recurrent surgical | 12 |
| Right recurrent injection | 5 |
| Left recurrent injection | 3 |
| Right recurrent injection done elsewhere | 1 |
| Right recurrent surgical 2 previous herniotomies | 6 |
| Left recurrent surgical 2 previous herniotomies | 2 |
| Left recurrent surgical and injection done elsewhere | 1 |
| | 261 |

It is realized that the diagnosis of indirect versus direct hernia by finger palpation has a large margin of error. The true diagnosis often can be proved only by operation.

The causes given by the patients for these hernias are as follows:

| | |
|---|---|
| Lifting | 129 |
| Unknown | 94 |
| Accident | 35 |
| Coughing | 3 |
| | 261 |

We were unable to trace 9 patients with 12 inguinal hernias. In this group there were 5 right and 1 left direct indirect, 3 left and 1 right indirect, 1 right and 1 left recurrent surgical.

Thus, the final number to be discussed is 205 patients with 249 inguinal hernias in whose cases there were 61 recurrences, listed as follows:

51 patients with 54 recurrent inguinal hernias
5 deceased patients with 5 recurrent hernias
2 patients sent questionnaires with 2 recurrent hernias

There were 22 patients with 26 hernias who died of intercurrent diseases. All but 6 of these patients were over 50 years of age. With the aid of their attending physicians and surgeons and the hospital records, I was able to learn the causes of death and listed them as follows: 15, cardiac disease; 4, carcinoma (2 pulmonary, 1 gastric and 1 rectal); 1, sarcoma of the neck; 1, cirrhosis of the liver, and 1, cerebral hemorrhage. Of the 26 hernias, there were no recurrences in 22, but there was 1 enlarged ring; there were 3 definite recurrences; and there was 1 questionable recurrence in a patient who was dead on arrival at a local hospital.

The 22 nonrecurrent inguinal hernias in the deceased patients are listed as follows as to the approximate number of years they were without recurrence before death:

| | | |
|---|---|---|
| 3 years | 3 | |
| 4 years | 3 | |
| 5 years | 1 | |
| 6 years | 5 | |
| 7 years | 5 | (1 enlarged ring) |
| 8 years | 4 | |
| 9 years | 1 | |

Those with recurrences were:

| | |
|---|---|
| 2 years | 1 |
| 6 years | 1 |
| ? years | 2 |

One hundred and sixty patients with 192 inguinal hernias were examined by other physicians and surgeons before coming to the office to receive the ambulant treatment. Of this number, 82 patients with 98 hernias were "insurance cases," and their fees for the injection therapy were paid for by 19 different insurance companies and 5 factories. Also, there were 4 employees (with 6 hernias) from the City of Springfield, which assumed responsibility for the cost of the treatments. All of the 160 patients covered by insurance came of their own volition.

All patients were examined personally except 5, to whom questionnaires were sent. These 5 patients had 6 hernias (1 right, 3 left direct indirect and 1 bilateral direct indirect). Four had no recurrences after ten years; 2 cases had recurrences, 1 after three years, and 1 patient did not know how many years he had had his recurrence, as he was symptom-free.

In the age group over 50 there were 86 patients with 103 inguinal hernias; i.e., 41.9 per cent of the patients had 40.9 per cent of these hernias. In the same age group, 20 patients (including those deceased) had 21 recurrent hernias; i.e., 23.2 per cent of these patients had a recurrent rate of 20.3 per cent.

There were 30 patients with 33 inguinal hernias who were seen after they had had a recurrence of a surgically repaired hernia. Twenty-five of these recurrent surgical hernias (including those of deceased patients) were without recurrences following the ambulant injection therapy after the following number of years:

| | |
|---|---|
| 3 years | 2 |
| 4 years | 1 |
| 6 years | 2 |
| 7 years | 3 |
| 8 years | 5 |
| 9 years | 5 |
| 10 years | 7 |

I was unable to trace 2 of these patients.

After the injection therapy, 6 patients with recurrent surgical hernias again had recurrences after the following number of years:

| | |
|---|---|
| 1 year | 1 |
| 3 years | 1 |
| 10 years | 2 |
| ? years | 2 |

Seven patients with 9 hernias, 6 of whom were treated at my office and 1 of whom was treated elsewhere prior to 1946, had recurrent injection hernias. The solution used was not Alparene No. 2. After the series of treatments with Alparene No. 2 there was 1 recurrence after seven years. Eight hernias were without recurrences after the following number of years:

| | |
|---|---|
| 8 years | 2 |
| 9 years | 1 |
| 10 years | 5 |

There was a recurrence in a patient who had undergone both operation and injection therapy, which was given elsewhere, and who was treated at my office in 1946. He had no recurrence after ten years.

In this series, 5 patients had had primary hernias (1 right indirect, 2 right and 2 left direct indirect) previously treated by injection in my office in the years 1937, 1938, 1942, 1943 and 1944 and were without recurrences. In 1946-48 they returned for the ambulant treatment of newly developed inguinal hernias in the opposite groin.

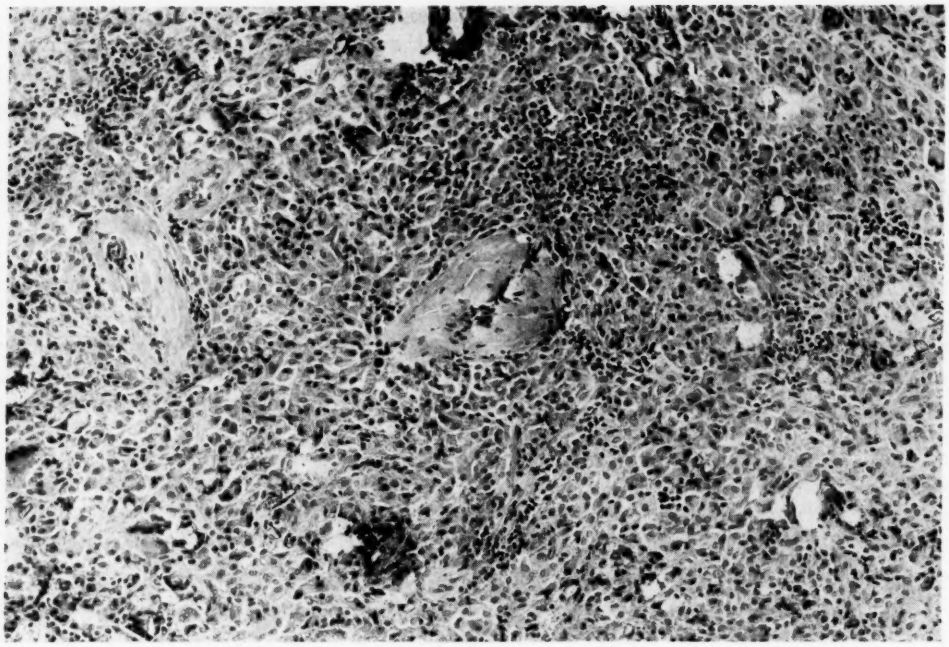


Fig. 3 (Case 4).—Low power photomicrograph (× 120), showing pronounced chronic granulomatous inflammatory reaction with foreign body giant cells. The tissue is almost totally composed of epitheloid cells with lymphocytes scattered in aggregates throughout.

Few children have been treated during the twenty years, and there were none in the 1946-1948 series. The treatment of 1 child, a boy aged 5 years, was satisfactorily completed, but he was a rare patient, being highly cooperative. Fewer treatments and smaller doses of the solution were used, along with a No. 22 bore short beveled needle.

### INDIVIDUAL STUDIES

CASE 1.—In 1947, a 32-year-old man who did much heavy lifting was given 24 injection treatments (44 cc. of Alparene No. 2 and 15 cc. of oil of sesame with 3 per cent phenol) for a left direct indirect inguinal hernia of two months' duration. On Sept. 29, 1950, he was operated upon at the Hartford (Connecticut) Hospital for a recurrence of the hernia. The operating room record read "a solid mass was removed, the size of an apple; some small lumps were present which had pus-like material in the center, which was due to the necrosis of the fibroplastic tissue." Frozen section "showed merely excessive fibrous or scar tissue reaction." Apparently, in this case, an excessive and concentrated amount of the asymmetric crystals were squeezed by the truss, muscular activity and tension producing a large amount of granulomatous tissue. The electrical impulses set up by the constant irritation of the concentrated and large amount of asymmetric crystals did not subside until a large mass had formed.

In 3 patients, who of their own volition had worn their trusses one to five years longer than the required time after completing their series of injections, large nongranular, nontender, solid masses developed in the treated groins. Evans and Zeit[12] stated, "Stress of some sort would hence be the functional stimulant where fibrosis is excessive."

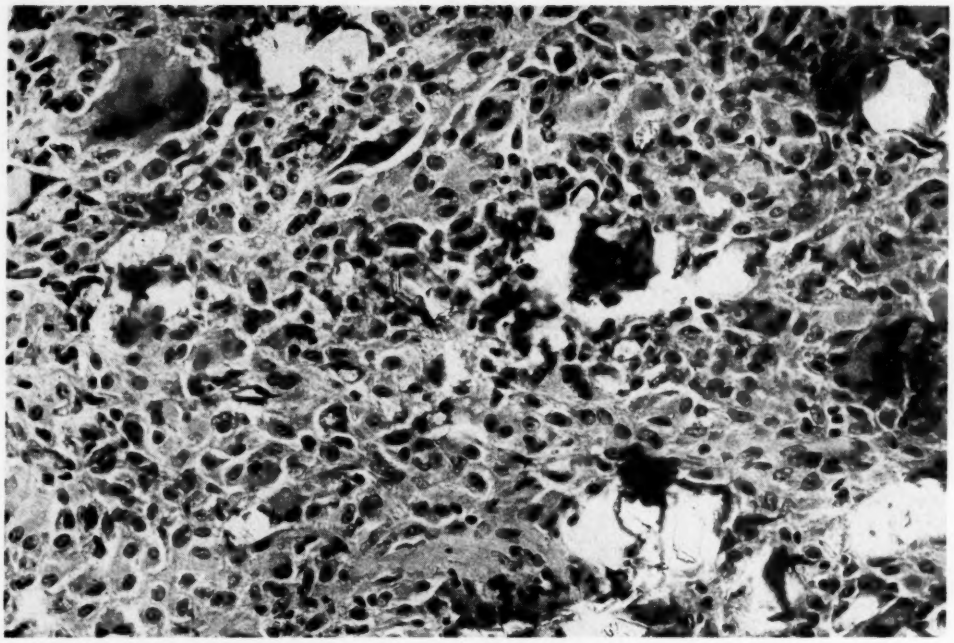


Fig. 4 (Case 4).—High power photomicrograph (× 280) of specimen shown in Figure 3. Note the crystalline foreign bodies among the epitheloid cells and often adjacent to the giant cells.

CASE 2.—In 1945, a 50-year-old man was examined and a diagnosis of a right direct indirect inguinal hernia was made. This was verified by the insurance company examiner. The patient's hernia was treated by the ambulant method, and he was then reexamined by the same insurance doctor, who found no evidence of a right inguinal hernia at that time. He stipulated, however, that he would not approve payment by the insurance company until a considerable time had elapsed after this examination. Four years later, in 1949, he again examined the patient and found no recurrence, so he approved payment. Three years later the patient entered the Springfield Hospital for surgical observation. On April 25, 1951, he was operated upon by his surgeon for chronic recurrent appendicitis. The operative record read: "Internal inguinal ring was found to be obliterated. Peritoneum of hernial sac was also obliterated totally."

CASE 3.—In 1945, a 46-year-old man stated that he had undergone right herniotomies in 1942, 1943 and 1944, each with a recurrence. He had had the injection treatment for the right recurrent surgical hernia given by me in 1945. Nine years later, on Dec. 12, 1954, he was admitted to the Massachusetts Soldiers Home in Holyoke to be operated or for an irregular, hard lumpy mass in the right groin and a right recurrent hernia. On December 13, with the region under spinal anesthesia, he was operated upon. The operative record read: "A large, irregular mass was removed from the right groin. Hesselbach's triangle was firm. No hernia was found." The pathologic diagnosis was foreign body granuloma.

CASE 4.—On Jan. 3, 1956, a 55-year-old man was admitted to the Springfield Hospital for removal of a right hydrocele of eighteen months' duration, possibly due to trauma. He stated that he had undergone a left herniorraphy in 1936 and had had a right inguinal hernia treated by the injection method by me in 1946. Physical examination revealed no evidence of recurrent hernia in either groin, but the patient had a large right hydrocele that could be transilluminated. On Jan. 4, 1956, with spinal anesthesia, the right hydrocele was excised. With the prior knowledge

and written consent of the patient, a biopsy specimen of the right groin was removed and was described as follows: "An incision was first made over Poupart's ligament and carried down to the aponeurosis of the external oblique. The entire granulomatous reaction was situated beneath the aponeurosis with the exception of the external ring where some reaction had occurred in the subcutaneous fat posterior to Scarpa's fascia. The external ring was entirely obliterated. The reaction could be palpated along the length of the inguinal canal to (approximately) the internal ring. The aponeurosis was incised along the length of the cord in this area, and a full thickness strip of aponeurosis down to the spermatic cord from internal to external ring was removed. The reaction was about ¼ inch thick at the region of the internal ring and about ½ inch thick at the external ring. It was noted that, for the most part, good planes of cleavage could be defined by sharp dissection over the aponeurosis and also over the spermatic cord. One could describe the granulomatous reaction as forming a tight glove about the spermatic cord. The pathologic diagnosis by Dr. William Kaufmann of this specimen, removed ten years after completion of the injection treatment, showed "foreign body granulomatous reaction containing a crystalline material" (Figs. 3 and 4).

CASE 5 (*Roentgen Data*).—In 1947, a 53-year-old man stated that he had had "lumps" in both groins for two years. During the same year, in my office, each of his direct indirect inguinal hernias was injected eighteen times, and the total amount used per groin was 26 cc. of Alparene No. 2 and 6 cc. of oil of sesame with 3 per cent phenol. Eight years later, on July 30, 1956, examination of both groins revealed no evidence of recurrences, and a moderate amount of granulomatous tissue was present in each groin. On the same day, roentgenologist Dr. John W. Turner took a survey film of the pelvic area, which showed "no difference in ossification of the pubic bones. There was no density observed in the inguinal areas to identify sites of the silicate injections."

*Sequelae and Complications.*—There have been no deaths among the 214 patients treated by injection in this series and no deaths with this procedure since I started treating inguinal hernias in this manner. Only 1 patient had an allergic reaction presumably due to an injection; "hives" developed but promptly disappeared after the administration of epinephrine. About 5 per cent of the 214 patients treated had a considerable amount of swelling and induration of the spermatic cord, which disappeared entirely within two to three weeks, aided by ice packs. Rarely was a patient sufficiently incapacitated to cause him to lose time from his daily routine.

There were no cases of local skin suppuration, inguinal abscesses or atrophied testes. Incidentally, during the first office visit, the testes are always examined along with the inguinal regions. On initial examinations, my 1946-1948 series revealed that about 4 per cent of the patients had atrophied testes on the same side as their hernias. Most of them stated that they had had mumps during childhood.

In the majority of cases, I have noted that post-injection recurrent hernias and their external rings were smaller than the original hernias.

Examination of this group of 214 patients revealed that 5 had small right hydroceles. Four had had direct indirect inguinal hernias and the other had a surgically recurrent hernia and stated that he had undergone two previous right herniotomies. Prior to this series and occasionally since 1948, a hydrocele did develop, usually following a deep injection. Unlike idiopathic and traumatic hydroceles, which often require surgical treatment, this post-injection type usually clears up permanently after one or two aspirations.

An excessive amount of nontender granulomatous tissue was produced in 23 patients with 26 inguinal hernias, and pronounced bulging was observed in the injected groins. In most cases it was undoubtedly due to the fact that some of the Alparene No. 2 had been injected into the subcutaneous fat anterior to the external

oblique aponeurosis before the needle was withdrawn. A nodular or granular feel was elicited in most of these groins. This deposition of the chemical into the subcutaneous fat rarely occurs now, as I ascertain the exact position of the needle point by the subfascial fulcrum test before withdrawing it from the inguinal canal. This has been done routinely for the past several years, and I make sure that the solution is injected entirely into the treated inguinal canal.

Alparene No. 2 has the faculty, when injected into subcutaneous fat, of forming small or large discreet nodules, which rarely become painful. If the chemical injected is highly concentrated or in too large an amount, these nodules or granules, at pathologic examination, may present centers with necrosis, liquefaction and calcification.

## COMMENT

"In communities in which the injection method has not been employed and may not even be known," Watson[13] advised, "the surgeon who contemplates the use of it, to discuss it with other doctors in his vicinity to familiarize them with it, so that if complications in the treatment should develop, he would not be charged with experimentation."

It is suggested that local surgeons acquaint themselves with the granulomas that form after the injection therapy. Some of the patients in this series have been advised by other surgeons to have emergency operations for "incarcerated hernias." It is not known how many of the patients who were treated by injection and later by operation may only have had a granuloma rather than a recurrent hernia. Such granulomas have also been mistaken for neoplasms and for tuberculosis.

It is understandable that, if a patient previously treated by injection is operated upon, the pathologist reports that a hernial sac was observed. The explanation of this, of course, is that the fibroplastic response against the injected material does not obliterate the sac, but either diminishes its width or holds it reduced within the internal ring. Thus, the resulting granuloma acts either as a buttress against the internal ring or as a tight glove about the hernial sac, or both. If now the granuloma is removed surgically, it stands to reason that a sac may be found and that repair is necessary. As a matter of fact, the sacs that have been examined have shown no significant reaction within the wall.

Possibly the application of roentgen rays, diathermy or ultrasonics to the human groin into which piezoelectric quartz crystals have been injected may increase ionization in tissue and enhance the effect of local fibrosis. This procedure might minimize the amount of material injected and still require very little roentgen dosage.

In 1953, Zimmerman and Anson[14] stated, "The final chapter on the sclerosing therapy of hernias has not yet, of course, been written."

## SUMMARY AND CONCLUSION

A series of 205 patients with 249 inguinal hernias treated by the ambulant injection method with Alparene No. 2 is presented.

The indications and prerequisites for successful therapy with this method are discussed in detail, and emphasis is laid upon the proper selection of cases for this type of therapy.

With this treatment there were 34 recurrences or 13.7 per cent within two years and 27 recurrences, or 10.8 per cent after intervals ranging from two to ten years. The end results at the end of eight to ten years showed 61 recurrences, or 24.5 per cent.

No evidence of the development of malignant charge on the basis of the ambulatory injection treatment has been encountered over the ten-year period of observation.

The conclusion is reached that there is a place for the ambulant injection method of treating inguinal hernia in the male.

**Author's Note:** I wish to thank the following doctors for their permission to use cases reported in this paper: Case 1, Dr. Lewis A. Giffen; Case 2, Dr. Carl M. Binnig, and Cases 3 and 4, Dr. Lester Frank.

I also wish to acknowledge the invaluable assistance of Velma L. Bosworth, R.N., and Cecelia M. Curylo, R.N., in obtaining the case data presented and the cooperation of Mr. Ronauld L. Trembly of the Vernon Surgical Shop, Springfield, Massachusetts, in the development and construction of the trusses described.

SUMARIO E CONCLUSOES

Uma serie de 205 pacientes com 249 hernias inguinais foi tratada em ambulatorio com injeções de Alparene n° 2.

Discute as indicações e requisitos para o sucesso terapêutico e salienta a correta seleção dos casos para este tipo de tratamento. Nesta serie houve 35 recidivas ou 13.7% dentro de 2 anos e 27 recidivas ou 10.8% depois de 2 a 10 anos.

Os resultados finais ao fim de 8-10 anos mostraram 61 recidivas ou sejam 24.5%.

Não houve transformações malignas na observação feita durante 10 anos. Chega a conclusão de que há um lugar na terapêutica das injeções como método ambulatorio de tratamento das hernias nos homens.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

Eine Serie von 205 Kranken mit 249 Leistenbrüchen wurde mit ambulanter Einspritzung des Präparates Alparele No. 2 behandelt.

Die Indikationen und die Voraussetzungen für eine erfolgreiche Behandlung mit dieser Methode werden im einzelnen erörtert. Auf die sorgfältige Auswahl der Fälle für diese Art der Behandlung wird besonderer Wert gelegt.

Bei dieser Behandlung kam es innerhalb von zwei Jahren zu 34 Rückfällen (13,7%) und nach zwei bis zehn Jahren zu 27 Rückfällen (10,8%).

Die Endergebnisse nach acht bis zehn Jahren zeigten 61 Rückfälle oder 24,5%.

Während der zehnjährigen Beobachtungszeit stellten sich keine Entwicklungen bösartiger Veränderungen auf Grund der ambulanten Injektionsbehandlung heraus.

Der Verfasser kommt zu dem Schluss, dass die ambulante Injektionsmethode in der Therapie der Leistenbrüche des Mannes ihren Platz hat.

RÉSUMÉ ET CONCLUSIONS

L'auteur présente une statistique de 205 malades atteints de 249 hernies inguinales, traités ambulatoirement par des injections d'Alparène No. 2.

Il décrit les indications et les conditions de succès de cette thérapeutique, qui exigent une bonne sélection des cas.

Il s'est produit 34 récidives (13.7%) au bout de deux ans, 17 récidives (10.8%) durant une période de deux à 10 ans, et 61 récidives (24.5%) après huit à dix ans.

Pendant un temps d'observation de dix ans il n'a été constaté aucune modification maligne due à cette thérapeutique. L'auteur en conclut qu'elle a sa place dans le traitement de la hernie inguinale chez l'homme.

RIASSUNTO E CONCLUSIONI

Viene presentata una serie di 205 casi di ernia inguinale curata con il metodo delle iniezioni ambulatorie di Alparene.

Vengono descritte in dettaglio le indicazioni e le carateristiche del metodo, sopratutto nei confronti della scelta dei malati.

Vi furono 34 recidive, pari al 13,7% entro i primi due anni e 27 (10,8%) fra il secondo e il decimo anno. In complesso vi furono 61 recidive (24,5%) al termine di un periodo di osservazione di 8-10 anni. Non vi furono casi di trasformazione maligna.

Nel maschio, pertanto, questo metodo può essere utilmente impiegato.

REFERENCES

1. Billroth, cited by Bratrud, A. F.: The Ambulant Treatment of Hernia, Ann. Surg. **105**:324-338, 1937.

2. Mayer, I.: Treatment of Hernia by Subcutaneous Injection, M. J. and Rec. **135**:275-278, 1932.

3. Valpeau, A. A.: New Elements of Operative Surgery. Translated by P. S. Townsend. N. Y.: A. A. & W. Wood, 1847, vol. 3, p. 554.

4. Cited by Koontz, A. R.: Present Status of the Injection Treatment of Hernia, Arch. Surg. **58**:273-278, 1949.

5. Cited by Dobson, L.: Late Results of Injection Treatment, Surgery 7:836, 1940.

6. Christopher, F.: Textbook of Surgery—4th Edition. Philadelphia: The W. B. Saunders Company, 1945, 4th ed., p. 1192. Present Status of Injection Treatment: Report of the Council on Pharmacy and Chemistry of the American Medical Association, J.A.M.A. **115**:533, 1940.

7. Koontz, A. R.: Present Status of the Injection Treatment of Hernia. Arch. Surg. **58**:273-280, 1949.

8. McNally, W. D., and Bergman, W. L.: Silicosis, Indust. Med. **4**:61-65, 1935.

9. Evans, S. M.: Tissue Responses to Physical Forces: 1. The Pathogenesis of Silicosis, A Preliminary Report, J. Indust. Hyg. and Toxicol. **30**:353-357, 1948.

10. Evans, S. M., and Zeit, W.: Tissue Responses to Physical Forces: The Response of Connective Tissue to Piezoelectrically Active Crystals, J. Lab. and Clin. Med. **34**:592-615, 1949.

11. Kaplan, L.: Granulomas Due to "Alparene No. 2" Used in Injection Treatment of Hernias, J.A.M.A. **151**:1180-1190, 1953.

12. Rice, C. O.: Injection Treatment of Hernias. Philadelphia: F. A. Davis and Company, 1937, pp. 146 and 123-125.

13. Watson, L. F.: Hernia. St. Louis: The C. V. Mosby Co., 1938, p. 558.

14. Zimmerman, L., and Anson, B. J.: Anatomy and Surgery of Hernia. Baltimore: The Williams & Wilkins Company, 1953, p. 150.

As long as the condition of the patient is such that the physician can cure him, the physican is obliged to do all that is necessary to improve and restore his patient's health. If, however, the physician decides on surgery as the best method of treatment, he is not authorized to proceed unless he has first secured his patient's consent. By operating he cannot avoid injuring the patient's body and will often cause permanent physical changes. If the patient is a minor, or mentally infirm, or insane, the physician's right to operate on the patient depends upon the consent of his legal representative.

When a patient's life is endangered by a disease that is progressive unless brought under control, to tell the patient the truth might deprive him of the spiritual energy necessary for recovery. Should such a reaction be an established medical experience, the physician is obliged *not* to inform the patient of the nature of the disease.

—*Honig*

# Tumors of the Renal Pelvis and Ureter

THEODORE R. FETTER, M.D., F.A.C.S., D.A.B., AND
J. LOUIS WILKERSON, M.D.

PHILADELPHIA, PENNSYLVANIA

THIS paper is based upon a study of 35 cases of carcinoma of the renal pelvis and ureter, 19 patients with tumors of the pelvis and 16 patients with tumors of the ureter. All of these patients were seen during the past twenty years, from 1936 through 1956, at Jefferson Hospital. Although we no longer consider either carcinoma of the ureter or carcinoma of the renal pelvis a rarity, they are relatively infrequent, and it therefore seems worth while to record our observations, particularly as regards the relation of the histologic type of the tumor to prognosis. It is not the purpose of this paper to attempt an exhaustive review of the literature or to discuss in detail the causation of these tumors, although a brief review of the observations up to the time of writing, as compared to our own observations, will be made.

*Incidence.*—Tumors of the renal pelvis and ureter are considered uncommon, although the incidence has increased decidedly during the past twenty-five years. This is undoubtedly due to increased awareness of these tumors and improved diagnostic methods. In 1955, Whitlock, McDonald and Cook stated that 312 cases of carcinoma of the ureter had been reported in the literature; since that time a number of cases have been added. Scott, in his review of tumors of the renal pelvis in Campbell's *Urology*, in comparing pelvic tumors to parenchymal tumors re-

TABLE 1.—*Age of Patient*

| *Age* | *Number* | *Pelvis* | *Ureter* |
|---|---|---|---|
| 20-29 | 2 | 1 | 1 |
| 30-39 | 4 | 1 | 3 |
| 40-49 | 5 | 5 | 0 |
| 50-59 | 7 | 3 | 4 |
| 60-69 | 7 | 4 | 3 |
| 70-79 | 3 | 1 | 2 |
| 80-90 | 1 | 1 | 0 |
| Unknown | 6 | 3 | 3 |
| Total | 35 | 19 | 16 |

TABLE 2.—*Site of Growth (Ureteral Tumor)*

| *Portion of Ureter* | |
|---|---|
| Upper third | 1 |
| Middle third | 0 |
| Lower third | 9 |
| Lower and middle thirds | 3 |
| Upper and lower thirds | 1 |
| All portions | 1 |
| Unknown (autopsy) | 1 |
| Total | 16 |

TABLE 3.—*Site Involved*

| | *Ureteral* | *Pelvic* |
|---|---|---|
| Right | 8 | 10 |
| Left | 6 | 9 |
| Unknown | 2 | 4 |
| Total | 16 | 19 |

From the Department of Urology, Jefferson Medical College and Hospital, Philadelphia.

Read at the Twenty-Second Annual Congress of the United States and Canadian Sections, International College of Surgeons, Chicago, Sept. 8-12, 1957.

Submitted for publication Sept. 13, 1957.

corded the incidence as 1:14 respectively.

*Age:* Both tumors of the pelvis and tumors of the ureter are most common in the fifth and sixth decades of life. There is a tendency for benign and low-grade tumors of the ureter to occur in younger persons. Table 1 illustrates the age distribution in our own series.

*Sex:* Both types of tumor are more common in the male than in the female, with a proportion of approximately 3:1. In this series there were 15 male and 4 female patients with tumors of the renal pelvis, 12 male and 4 female patients had tumors of the ureter.

*Site of Growth:* Study of the cases previously reported reveals that most (two-thirds or more) of the ureteral tumors occur in the lower third of the ureter. A significant percentage of both types of tumore are multiple, probably about 25 per cent. In this series, 13 of 16 ureteral tumors involved the lower third, 4 of these involving both the middle and lower thirds (Table 2).

Tables 11 and 12 illustrate the multiplicity of tumors in this series, 7 of 19 tumors of the renal pelvis and 11 of 16 ureteral tumors being multiple.

Some reports have stated that the right side is involved somewhat more often than the left. This was not, however, the experience of Whitlock, McDonald and Cook, who found, in a review of 33 patients with carcinoma of the ureter, that the left side was involved 21 times and the right side 12 times. Table 3 illustrates the side involved in this series, there being no significant difference.

*Symptoms.*—The majority of patients complain of hematuria, this having previously been found to be present in about 70 per cent of the cases. A lesser percentage (about 60 per cent) in a recent series by Cook, Culp, McDonald and Utz complained of lumbar or abdominal pain. Dysuria and frequency of urination are

TABLE 4.—*Presenting Symptom—Carcinoma of Renal Pelvis and Ureter*

| | *Hematuria* | | *Lumbar Pain* | | *Abdominal Pain* | | *Frequency* | | *Dysuria* | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Duration* | *Ureter* | *Pelvis* | *Ureter* | *Pelvis* | *Ureter* | *Pelvis* | *Ureter* | *Pelvis* | *Ureter* | *Pelvis* |
| Less than 1 week | 3 | 4 | 1 | | | 2 | | | | |
| Less than 1 month | 1 | 2 | 1 | | | | | | 1 | |
| 1-3 months | 2 | 5 | | 3 | | | | | | |
| 3-6 months | 1 | 1 | 2 | | | 1 | | | | |
| 6-12 months | 1 | 1 | | | | | | 1 | 1 | 1 |
| 1-2 years | | | | 1 | | | | | | |
| 2-3 years | | | 1 | | | | | | | |
| 3-4 years | | | | | | | | | | |
| 4-5 years | 1 | | | | | | | | | |
| 6-7 years | | | 1 | | | | | | | |
| 16 years | 1 | | | | | | | | | |
| 31 years | | | 1 | | | | | | | |
| Totals | 10 | 13 | 7 | 4 | 0 | 3 | 0 | 1 | 2 | 1 |

Symptoms Unknown:
Carcinoma of the pelvis—4
Carcinoma of the ureter—3

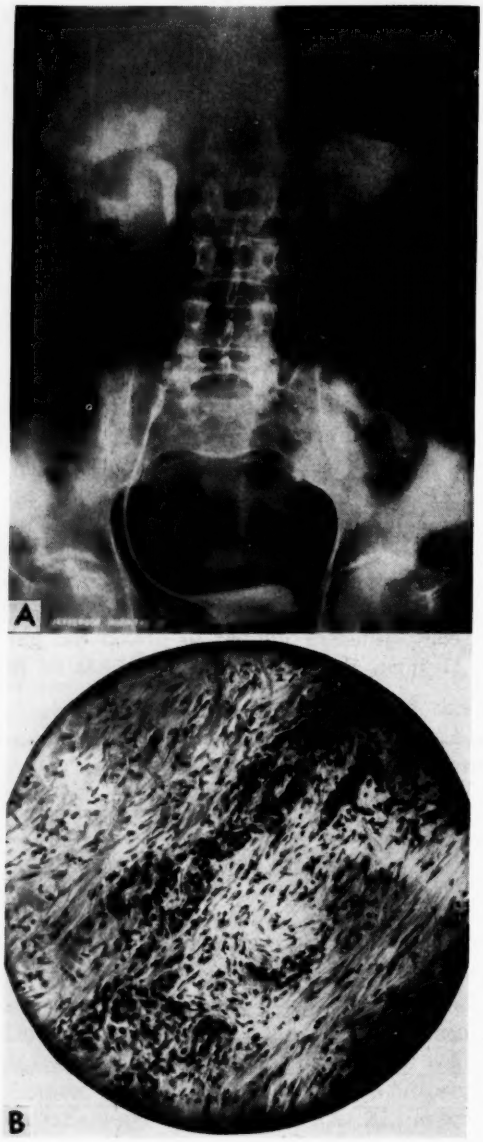



Fig. 1.—*A*, retrograde pyelogram showing filling defect in lower and middle calyceal systems. *B*, histologic section showing poorly differentiated squamous cell carcinoma of the renal pelvis (× 200), in a 63-year-old white man who died fifteen months after nephrectomy, of metastasis; the patient also had a squamous cell carcinoma of the bronchus, for which pneumonectomy was done. It could not be determined whether two primary carcinomas existed, or whether one was metastatic.

occasional complaints. An abdominal mass is occasionally noted by the patient. In this series, 10 of 16 patients with carcinoma of the ureter had a history of hematuria (62.5 per cent), and 13 of 19 patients with carcinoma of the pelvis had hematuria (67.7 per cent). Of the patients with ureteral tumors, 7 of 16 (43.75 per cent) complained of lumbar pain. Table 4 presents the clinical symptoms and their duration in this series. It is interesting to note that 1 patient had hematuria intermittently for four or five years and another for sixteen years. It seems likely that each of these 2 patients may have had a benign, slow-growing, tumor that later underwent malignant change.

*Diagnosis.* — *Cystoscopic*: The cystoscopic data should often lead one to suspect the diagnosis. In some patients with carcinoma of the ureter the tumor may be seen to protrude from the ureteral orifice. This occurred in 6 of the 16 cases of ureteral carcinoma in this series. The presence of a vesical tumor, especially one situated near the ureteral orifice or on the base of the bladder, should make one think of the possibility of tumor in the upper part of the tract. Edema and congestion, occasionally associated with dilatation, sometimes involve the affected ureteral orifice. The excretion of phenolsulphthalein or indigo carmine is often decreased or absent on the affected side. The presence of these signs in this series is indicated in Table 6, 12 of the 16 ureteral tumors and 7 of the 19 pelvic tumors having been associated with significant cystoscopic observations.

Two patients with primary carcinoma of the renal pelvis and secondary involvement of the lower part of the ureter also had tumor protruding from the ureteral orifice. The egress of bloody urine from the ureteral orifice on the involved side is often observed, although it was only noted 7 times in this series of 35 cases.

TABLE 5.—*Roentgen Data*

| | *Carcinoma of Ureter* | *Carcinoma of Renal Pelvis* |
|---|---|---|
| Filling defect with or without deformity | 6 | 12 |
| Hydronephrosis and hydroureter | 3 | |
| Hydronephrosis | 2 | 2 |
| Hydroureter | 1 | |
| Non-function of kidney on intravenous urogram | 3 | 2 |
| Calculi | | 2 |
| Normal roentgen picture | 3 | |
| Unknown | 3 | 5 |
| Totals | 21 | 23 |

TABLE 6.—*Cystoscopic Data*

| | *Bloody Urine from Orifice* | *Tumor Protruding from Orifice* | *Bladder Tumor* | *Dilated Orifice* |
|---|---|---|---|---|
| Ureter | 4 | 6 | 1 | 1 |
| Pelvis | 3 | 2 | 1 | 1 |
| Totals | 7 | 8 | 2 | 2 |

TABLE 7.—*Carcinoma of Ureter: Incidence of Types and Grades*

| *Grade* | *Papillary* | *Papillary and Infiltrating* | *Infiltrating* |
|---|---|---|---|
| 1 | 5 | 0 | 0 |
| 2 | 1 | 4 | 0 |
| 3 | 0 | 3 | 2 |
| 4 | 0 | 0 | 1 |
| Totals | 6 | 7 | 3 |

Scott, in *Campbell's Urology*, stated that tumor of the bladder is present in 20 to 25 per cent of the patients with carcinoma of the renal pelvis; similarly, it is present in a significant number of patients with ureteral carcinoma. In 1 of the cases in this series the diagnosis of carcinoma of the ureter was not made for two years after the patient was treated for carcinoma of the bladder, despite the initial

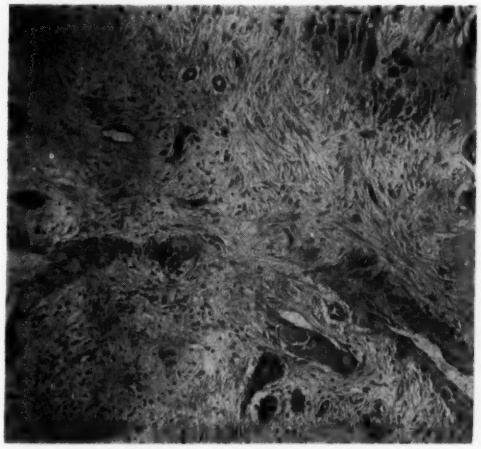


Fig. 2.—Histologic section showing squamous cell carcinoma of renal pelvis with infiltration into parenchyma. × 67.

presence of mild hydroureter on the intravenous urogram. This patient died of metastasis three years and eight months after a diagnosis of vesical carcinoma was made; the ureteral tumor was diagnosed as papillary carcinoma, Grade II, without infiltration, whereas the vesical carcinoma was a papillary carcinoma, Grade III, with infiltration.

Catheterization of the involved ureter often reveals complete obstruction in the tumor area. In some instances the catheter may be passed but its passage is followed by bleeding from the ureteral orifice around the catheter, or bleeding through the catheter, the latter usually disappearing when the tumor area is passed.

*Roentgen Studies*: Excretory urographic studies reveal significant signs in the majority of cases. Hydronephrosis and hydroureter are common. A filling defect in the involved area, often of the "goblet-shaped" variety, is frequently seen, or the involved area may appear as a point of stricture in the ureter. Decreased or absent function is common. The roentgenographic data on this series are

Fig. 3.—Histologic section showing papillary cystadenocarcinoma of renal pelvis. × 100. Patient was a 35-year-old white woman with a complaint of hematuria; retrograde pyelogram demonstrated filling defect in renal pelvis. Patient died of metastases thirty-nine months after operation. (*Courtesy of Dr. David M. Davis.*)

TABLE 8.—*Carcinoma of Renal Pelvis: Incidence of 4 Types and Grades*

| *Grade* | *Papillary* | *Papillary and Infiltrating* | *Infiltrating Carcinoma* | *Mucous Adenocarcinoma* | *Papillary Adenocarcinoma* |
|---|---|---|---|---|---|
| 1 | 1 | 0 | 0 | 0 | 0 |
| 2 | 4 | 3 | 0 | 0 | 0 |
| 3 | 0 | 3 | 4 | 1 | 1 |
| 4 | 0 | 0 | 2 | 0 | 0 |
| Totals | 5 | 6 | 6 | 1 | 1 |

recorded in Table 5. It is significant that the roentgen signs are positive in the majority of cases.

*Etiologic and Pathogenic Background.*—It is not within the scope of this article to deal with an exhaustive review of the literature concerning the etiologic factors. Much has been said previously of the etiologic theories advanced. Maclean and Fowler, as well as many others have pointed out that proliferative or metaplastic changes may take place as a result of chronic irritative changes in the ureter or pelvis. Proliferative changes include ureteritis granulosa, pyelitis granulosa, ureteritis polyposa and pyelitis polyposa. If there is a downward proliferation of the epithelium, however, solid nests of cells may be seen, as originally described by von Brunn in 1893. This may result in ureteritis cystica or pyelitis cystica. Fagerstrom made a detailed study of ureters removed from 120 cadavers in order to study epithelial aberrancies and to determine the possible etiologic significance in cases of tumor of the ureteral mucosa. He concluded that the epithelial buds and crypts were bizarre expressions of epithelial hyperplasia and was unable to support the theory of "cell nest" formation proposed by von Brunn. Fagerstrom was unable to develop any evidence that solid epithelial buds are directly associated with the origin of solid tumors of the urinary epithelium. Maclean and Fowler pointed out that both squamous and mucinous metaplasia may take place, and presented patients illustrating these changes. They mentioned, as irritants that may produce proliferative or metaplastic changes, (1) long-continued bacterial infection, (2) obstructive uropathic conditions, (3) calculus, (4) avitaminosis, especially of vitamin A, (5) hormonal imbalance (6) toxic products of metabolism and (7) specific carcinogens. They reported the fourth case of mucinous adenocarcinoma of the renal pelvis. The fifth case of such a tumor is presented as a part of this series, as are 3 cases of squamous cell carcinoma of the renal pelvis. Etiologic factors that ex-

plain the multiplicity of ureteral tumors are lymphatic permeation, surface implantation and multicentric origin. Most observers agree that a multicentric agent is responsible for the stimulation of the multiple tumors that may appear in the urinary tract. There seems to be little pathologic support for lymphatic permeation. Various investigators have been unable, for the most part, to transplant tumor cells in the experimental animal, which argues against surface implantation. On the other hand, surface implantation is supported by the fact that the tumors usually seem to follow the flow of urine and to be most common in the area of the ureter where temporary stasis is present. Bothe, in 1943, studied 6 tumors of the ureter and 4 of the renal pelvis, stated that he observed similar changes

TABLE 9.—*Operations Performed for Ureteral Tumor*

| | |
|---|---|
| Nephro-ureterectomy with cuff of bladder | |
| One-stage | 8 |
| Two-stage | 3 |
| Nephrostomy (metastatic carcinoma) | 1 |
| Cystoscopic removal and fulguration | 3 |
| No operation (inoperable) | 1 |
| Total | 16 |

TABLE 10.—*Operations Performed for Tumor of Renal Pelvis*

| | |
|---|---|
| Nephro-ureterectomy with cuff of bladder | |
| One-stage | 3 |
| Two-stage | 5 |
| Nephrectomy and partial ureterectomy | 8 |
| Unknown | 2 |
| No operation | 1 |
| Total | 19 |

TABLE 11.—*Carcinoma of the Renal Pelvis; Multiple Growths*

| | |
|---|---|
| Renal pelvis and lower third of the ureter | 3 |
| Renal pelvis and bladder | 2 |
| Renal pelvis and proximal third | 1 |
| Renal pelvis, proximal and distal thirds | 1 |
| Total | 7 |

TABLE 12.—*Carcinoma of the Ureter; Multiple Growths*

| | |
|---|---|
| Lower third and bladder | 5 |
| Lower and middle thirds | 3 |
| Upper and lower thirds | 1 |
| All portions | 1 |
| Unknown | 1 |
| Total | 11 |

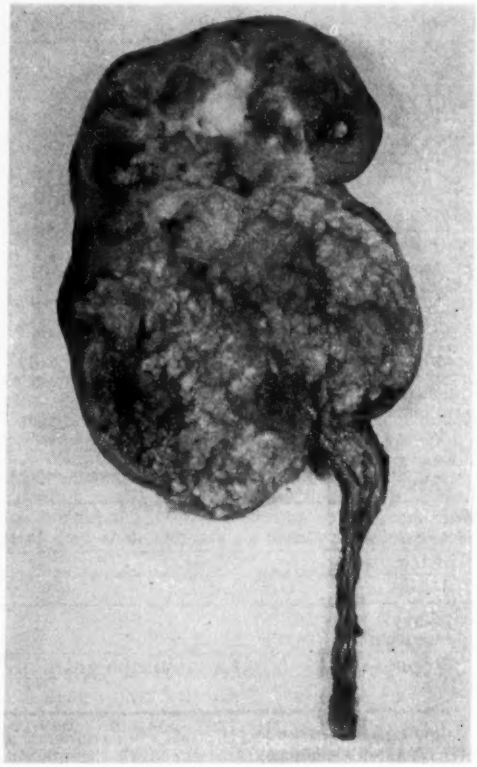


Fig. 4.—Gross specimen showing invasive papillary carcinoma of renal pelvis and upper part of ureter; lower part of ureter (not shown) was also involved. Patient was a 42-year-old white man who underwent nephroureterectomy with excision of a bladder cuff; he remained well for five and one-half years. Recently he had a recurrent papillary carcinoma of the bladder.

TABLE 13.—*Carcinoma of the Renal Pelvis: Survival*

| | 0-1 Yr. | 1-2 Yr. | 2-3 Yr. | 3-4 Yr. | 4-5 Yr. | 5-10 Yr. | More than 10 Yr. |
|---|---|---|---|---|---|---|---|
| Papillary transitional cell carcinoma, no infiltration | | | | | | | |
| Living | | | | | | 2* | |
| Dead | | | | | | | |
| Unknown | 3 | | | | | | |
| Papillary transitional cell carcinoma, infiltrating | | | | | | | |
| Living | | 3 | | | | | |
| Dead | | | | | | | 1** |
| Unknown | 2 | | | | | | |
| Infiltrating carcinoma | | | | | | | |
| Living | | 1 | | | | | |
| Dead | 1† | 2 | | 1 | | | |
| Unknown | 1 | | | | | | |
| Mucoid adenocarcinoma | | | | | | | |
| Living | | | | | | | |
| Dead | 1 | | | | | | |
| Papillary adenocarcinoma | | | | | | | |
| Living | | | | 1 | | | |
| Dead | | | | | | | |

*Now has recurrent small papillary carcinoma of the bladder.
**Died after eleven years of coronary thrombosis.
†No operation; died in the hospital of metastasis.

TABLE 14.—*Carcinoma of the Ureter: Survival*

| | 0-1 Yr. | 1-2 Yr. | 2-3 Yr. | 3-4 Yr. | 4-5 Yr. | 5-10 Yr. | More than 10 Yr. |
|---|---|---|---|---|---|---|---|
| Papillary carcinoma; no infiltration | | | | | | | |
| Living | | | | | | 1 | 2 |
| Dead | 1** | 1‡ | | | | | |
| Papillary, infiltrating | | | | | | | |
| Living | | 2 | 1 | 1 | | | |
| Dead | 1§ | | 1 | 1 | | | |
| Infiltrating | | | | | | | |
| Living | | | | | | | 1† |
| Dead | 1* | | | | | | |

Unknown, 2 (1 papillary, 1 infiltrating).
*Metastatic carcinoma of the cervix.
**Postoperative death (sixteen days).
†Died of coronary thrombosis more than ten years after a nephroureterectomy with cuff of bladder.
‡Died of causes other than carcinoma.
§No operation; died of metastasis.

proximal and distal to the tumor site and described areas of round cell infiltration, epithelial thickening, submucosal hyperemia and papillary formation. He concluded that the inflammatory areas "illustrated early reaction to carcinogenic stimulation, while areas of proliferating basal cells were more advanced lesions eventually becoming papillary and definitely neoplastic." Keen studied 5 surgical specimens, 3 tumors of the ureter and 1 tumor of the renal pelvis for evidence of subepithelial inclusions, but could detect only nonspecific inflammatory changes.

*Pathologic Picture.* — Numerous classifications for tumors of the pelvis and ureter have been suggested. Twenty-two categories or diagnoses were given in Scott's review of 182 cases. A far simpler and more workable and logical classification of tumors of the renal pelvis, however, was proposed by McDonald and Priestley in 1944: papillary carcinoma; papillary carcinoma with infiltration, and infiltrating carcinoma. They studied a group of 75 patients and observed 27 papillary carcinomas, 25 papillary carcinomas with infiltration and 23 infiltrating carcinomas without the formation of villous fronds. The first group included tumors characterized (a) by villous fronds projecting into the lumen of the pelvis and (b) by lack of muscular infiltration. The papillary and infiltrating group included those in which the tumor had invaded the muscle of the pelvis, the peripelvic tissue or the kidney. The third group included those tumors in which the neoplastic cells infiltrated the tissue adjacent to the pelvis but in which there was no formation of villous projections. In 1954 Whitlock, McDonald and Cook presented a similar classification for carcinoma of the ureter, which was as follows: (a) papillary carcinoma, Grades I, II and III; (b) papillary and infiltrating carcinoma, Grades II, III and IV, and (c) nonpapillary infiltrating carcinoma, Grades II, III and IV.

Fig. 5.—Gross specimen showing mucinous adenocarcinoma of renal pelvis. Involvement of perirenal fat and parenchymal invasion were present. Patient was a 57-year-old white man who had a known renal calculus for twenty-three years; he also complained of intermittent lumbar pain and, three months prior to admission passed a small calculus, accompanied by some hematuria. There was no renal function according to urogram. Patient died of metastasis six months after nephrectomy.

These careful and valuable studies proved the need for such a classification, since the authors demonstrated that in most cases the prognosis was directly related to the histologic appearance of the tumor. McDonald and Priestley listed as living 13 of 25 operated on for papillary carcinoma, 3 of 18 patients living with infiltrative papillary carcinoma, and only 1 living patient of 14 traced who were operated on for infiltrating carcinoma—a five-year survival rate of 52, 16.7 and 7.1 per cent respectively. A similar study by Whitlock, McDonald and Cook demonstrated survival rates at five years of 66.7 and 14.3 per cent and no survivals among patients with papillary, papillary infiltrating, and nonpapillary infiltrating carcinomas of the ureter, respectively. Thirty-three cases of primary carcinoma of the ureter were studied in the latter series. This study has followed the pathologic classification used by McDonald and Priestley. Tables 7 and 8 indicate the in-

Fig. 6.—Histologic section showing papillary carcinoma, Grade 2, with invasion of lymphatics and superficial subpelvic involvement. × 67. Patient was a 43-year-old white man who complained of painless hematuria; cystoscopic study demonstrated bloody urine coming from ureteral orifice, and retrograde pyelographic study demonstrated a filling defect in the renal pelvis and superior calyx. Complete nephroureterectomy with excision of a cuff of bladder was performed. (*Courtesy of Dr. David M. Davis.*)

cidence of the types and grades of tumor observed in this series.

It is to be noted that 1 case of mucinous adenocarcinoma of the renal pelvis and 1 case of papillary adenocarcinoma of the renal pelvis were encountered.

Mucinous adenocarcinoma has previously been reported (total of 4 cases) by Plaut, Ackerman, Ragins and Rolnick and by Arcadi. In 3 of the four cases renal calculi were reported to have been present, and in the fourth their presence was considered probable on the basis of history. Our patient also had chronic pyelonephritis and nephrolithiasis; the latter was known to have been present for twenty-two years. This type of renal tumor undoubtedly arises as a result of metaplasia from chronic infection and calculi. It is to be noted that, in our patient, the question arose of origin of the mucinous adenocarcinoma from the gastrointestinal tract, but no evidence was found for this.

Papillary adenocarcinoma of the renal pelvis is also a rare tumor and is thought to arise from metaplastic epithelium. Jacob and Mau reported the case of a 57-year-old white man who had such a tumor, associated with a large renal calculus. Our patient did not have a calculus and had apparently been in good health, without urologic complaints.

*Metastatic Tumors of the Ureter.*—Excluding those tumors which extend directly from pelvic organs, specifically uterus, bladder and prostate, and also extension from carcinoma of the renal pelvis, secondary involvement of the ureter is relatively rare. Presman and Ehrlich in 1948 reported 2 cases of metastatic involvement of the ureter and reviewed the 35 cases previously reported. The primary sites were listed as follows for the 37 patients: stomach and prostate, 8 each; generalized lymphoma, 4; cervix, 3; bladder, breast, lung, large bowel and ovary, 2 each, and ureter, vagina, uterus and urethra, one each. In 50 per cent of these cases there were symptoms referable to involvement of the ureter, 17 of the patients (46 per cent) having lumbar pain, 9 (24 per cent) having an elevated blood urea or nonprotein nitrogen levels and 6 (16 per cent) having anuria. The histologic character of these metastatic lesions was reported as follows:

| | |
|---|---|
| Adenocarcinoma | 22 |
| Squamous cell carcinoma | 6 |
| Sarcoma | 3 |
| Hodgkin's disease | 2 |
| Transitional cell carcinoma | 2 |
| Nonspecified | 2 |

The diagnosis has usually been made at postmortem examination, and the most common sites of the primary lesion have been the prostate and stomach. In 90 per cent of the cases there were metatases in other organs, and bilateral ureteral metas-

tases occurred in 60 per cent of the cases. The present series includes 1 patient with metastatic carcinoma of the cervix. Actual involvement of the ureter from the cervix with metastatic carcinoma is quite rare. Henriksen in 1949 reported a study

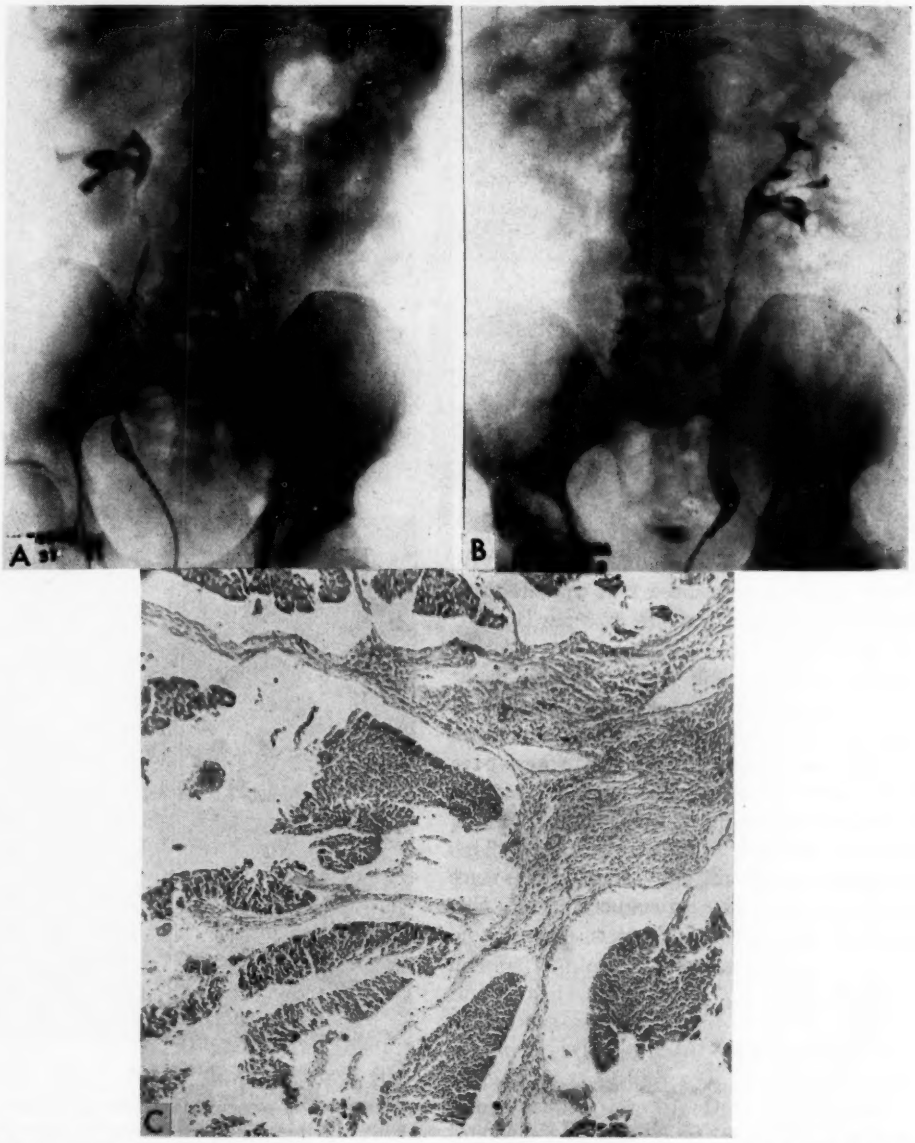



Fig. 7.—*A*, right retrograde pyelogram demonstrating filling defect in superior calyx. *B*, left retrograde pyelogram, normal except for dilatation of the lower part of the ureter. *C*, histologic section showing papillary carcinoma, Grade 2, with no invasion. × 50. Patient was a 69-year-old white man with painless hematuria; he underwent a two-stage nephroureterectomy with excision of a bladder cuff and survived eleven years, dying of causes other than carcinoma.

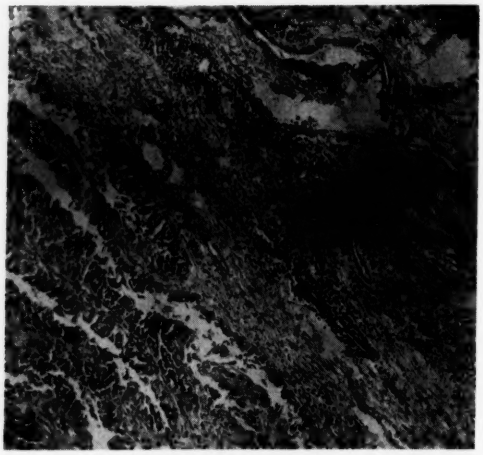


Fig. 8.—Histologic section showing papillary carcinoma of the renal pelvis, Grade 2; no infiltration present. × 67.

of 420 necropsies in which the primary disease had been carcinoma of the cervix. He stated that the frequency of distant metastases in cases of carcinoma of the cervix is not widely appreciated and that distant metastases had occurred in 32.5 per cent of the non-treated and 37.8 per cent of the treated tumors. The liver was the most frequent site of metastasis with the bone, lung and bowel involved in that order. Unusual sites included the brain and primary involvement of the ureter; the author observed primary involvement of the ureter in 2.1 per cent of the cases. The following classification, which seems entirely adequate, is reproduced from the work of Maclean and Fowler.

**Tissue of Origin**

A. *Epithelial*
   Gross
      Papillary, 75 per cent
      Solid, 25 per cent
   Microscopic (Whitlock, McDonald & Cook—1954) *Note*:

| | |
|---|---|
| 1. Papillary carcinoma, Grades 1, 2, 3 | 1. Structural type (papillary or nonpapillary) |
| 2. Papillary and infiltrating carcinoma, Grades 2, 3, 4 | 2. Presence or absence of infiltration |
| 3. Non-papillary infiltrating carcinoma, Grades 2, 3, 4 (including transitional cell carcinoma, squamous cell and adenocarcinoma) | 3. Cell type (transitional or squamous) |
| | 4. Degree of anaplasia |

B. *Mesodermal*
   Benign fibroepithelial polyp:
      Myoma
      Lipoma
      Neurofibroma
      Angioma
   Malignant
      Fibrosarcoma
      Myosarcoma
      Lymphoblastoma
C. *Endometriosis*
D. *Metastatic*

*Endometriosis of the Ureter.*—This condition is quite rare. One case has been observed at Jefferson Hospital but is not included in this series. It is mentioned only because of the possibility of confus-

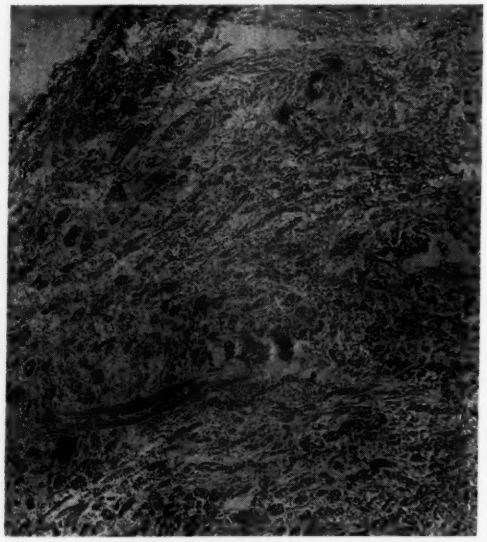


Fig. 9.—Papillary carcinoma of the ureter, infiltrative, Grade 4, with involvement of lymph channels and muscularis. Patient was a 55-year-old white man with hematuria and dysuria of one year's duration. Intravenous urogram was normal, but cystoscopic study showed tumor protruding from ureteral orifice. Patient died of coronary thrombosis more than ten years after two-stage nephroureterectomy with excision of bladder cuff. (*Courtesy of Dr. David M. Davis.*)

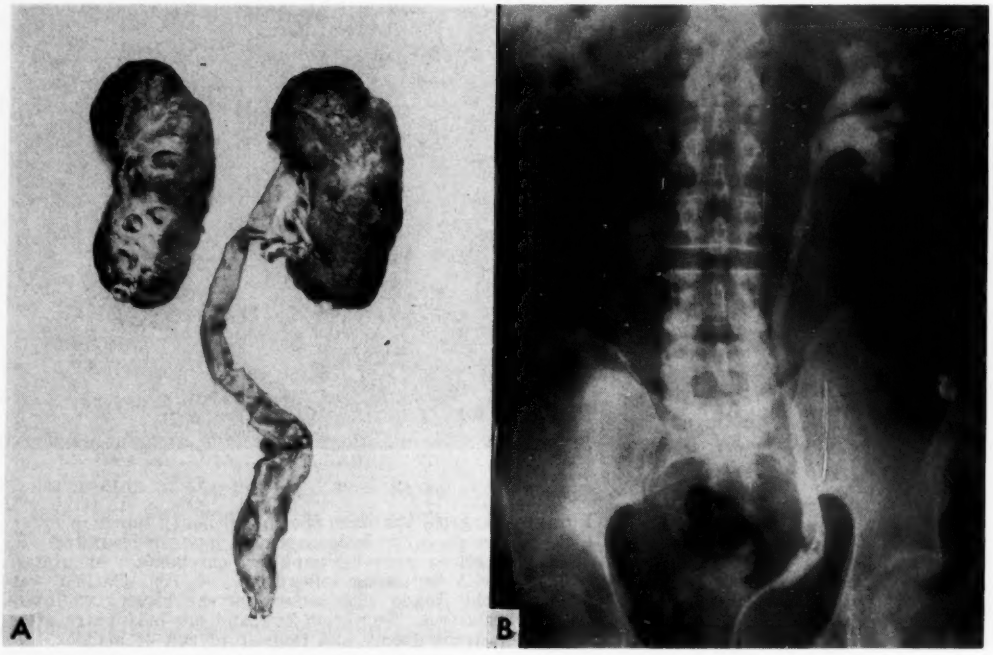



Fig. 10.—*A*, gross specimen showing primary carcinoma in lower third of ureter, associated with hydronephrosis and hydroureter. *B*, retrograde pyelogram, same patient, showing filling defect in the lower ureter. Patient was a 58-year-old white man with hematuria of six weeks' duration. Intravenous urogram demonstrated decreased function on affected side, some hydronephrosis and hydroureter. Cystoscopic study showed tumor protruding from ureteral orifice. Complete nephroureterectomy with excision of a bladder cuff was done. Histologically there was papillary carcinoma of the ureter, Grade 2, with superficial muscularis invasion. Patient surviving one year after operation.

ing the condition with a primary ureteral tumor. In 1941 Randall reported the first case with involvement of the ureter; O'Conner and Greenhill, in 1945, reported a second case with involvement of the ureter, in addition to an endometrioma of the bladder. In both cases there was ureteral filling defects, gross hematuria, renal pain, urgency and frequency of urination and nocturia. In neither case was a cyclic type of bleeding present.

Hodgkin's disease involving the ureter has been observed 3 times during the past several years at Jefferson Hospital. These 3 cases are not included in this series but will be the subject of a future study.

*Treatment.*—It is now accepted that complete nephroureterectomy and partial cystectomy is the operation of choice. Should the patient's general condition be poor, the two-stage operation may be used, preferably with removal of the tumor area at the time of the first operation. Conservative treatment for tumors of the pelvis and ureter is not recommended, unless the preservation of renal function is imperative. In this connection, Colston and Arcadi in 1954 reported the successful surgical excision of a papillary tumor of the renal pelvis in a patient with a single functioning kidney, and subsequent removal of the opposite kidney for papillary tumor of the pelvis. Colston described a similar patient of Gibson's, who had previously undergone ne-

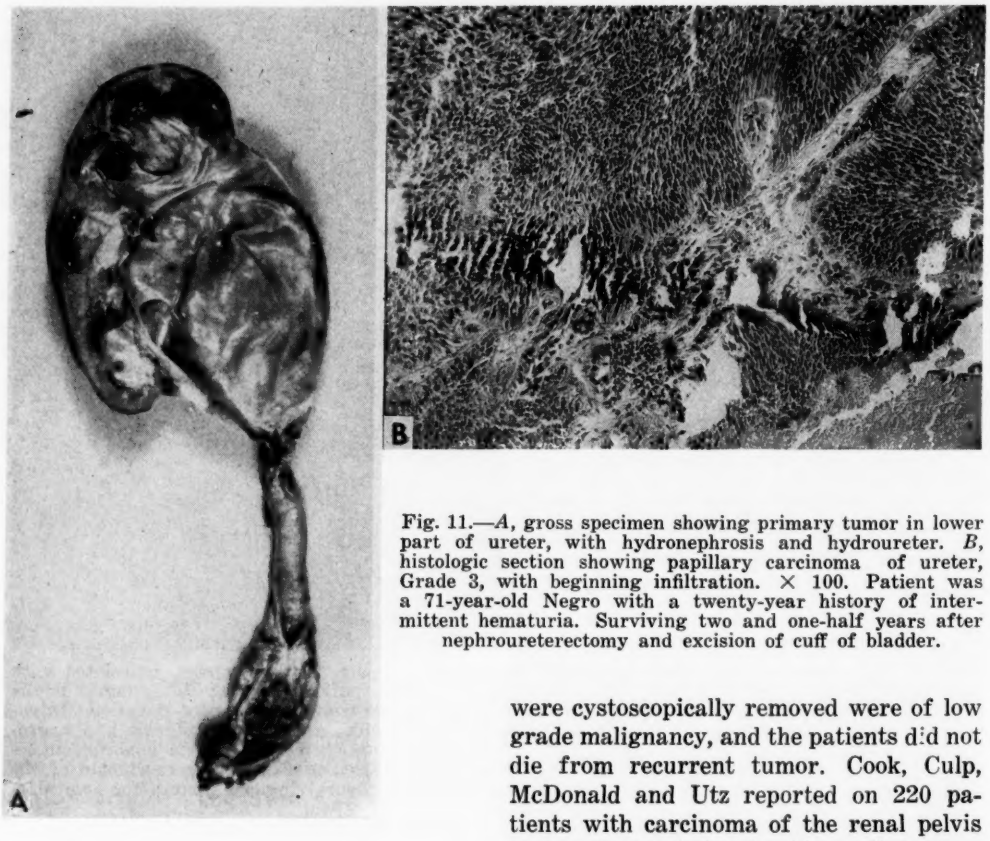



Fig. 11.—*A*, gross specimen showing primary tumor in lower part of ureter, with hydronephrosis and hydroureter. *B*, histologic section showing papillary carcinoma of ureter, Grade 3, with beginning infiltration. × 100. Patient was a 71-year-old Negro with a twenty-year history of intermittent hematuria. Surviving two and one-half years after nephroureterectomy and excision of cuff of bladder.

phrectomy for papillary carcinoma of the pelvis. In 1948 Ferris and Daut reported the case of a patient similarly treated, who had a solitary kidney and who survived for seven years. Nephrectomy with partial ureterectomy only is associated with a significant percentage of residual or recurrent tumors in the lower part of the ureter. One patient in this series underwent nephrectomy with partial ureterectomy and was later observed to have tumor in the ureteral stump, after which she consented to ureterectomy and partial cystectomy and has remained well. The operations performed in this series are outlined in Tables 9 and 10.

All 3 tumors of the ureteral orifice that were cystoscopically removed were of low grade malignancy, and the patients did not die from recurrent tumor. Cook, Culp, McDonald and Utz reported on 220 patients with carcinoma of the renal pelvis and ureter treated at the Mayo Clinic from 1910 through 1954. They noted that 43 per cent of the patients who underwent complete nephroureterectomy had subsequent tumors of the bladder. This was true also in several cases in our series. A higher percentage of patients treated by nephrectomy and partial ureterectomy had had recurrent tumors either in the bladder or in the remaining ureteral stump.

*Prognosis.*—In 1956 Dees published his observations as to the prognosis of primary tumors of the renal pelvis and ureter. He stated that he had encountered considerable difficulty in tabulating the material, since many of the factors, including the exact type of operation, the presence or absence of metastases at time

of operation and adequate follow-up studies, were at times impossible to obtain. Dees reported on 22 patients with primary tumors of the renal pelvis and ureter seen at Duke Hospital, with the following results:

> In four cases of transitional cell carcinoma of the pelvis the patients were living six, seven, eight and eighteen years respectively after operation (seven-year survivor had a recurrent tumor in the bladder).
>
> Five patients died within one year of operation and another within two years.
>
> Of two patients with squamous cell carcinoma of the pelvis, 1 was living less than two years after the operation and the other died within one year.
>
> Two patients with benign papilloma of the pelvis were living eight and fifteen years, respectively, after the operation. Of 8 patients with transitional cell carcinoma of the ureter, 4 were known to be living, but for less than one year after the operation.

The very excellent study of Scott in 1943 reported that 32 of 149 patients were well when last seen, but only 6 had been performed. Despite "low grade" nature of both tumors, the patient died of metastasis on September 30.

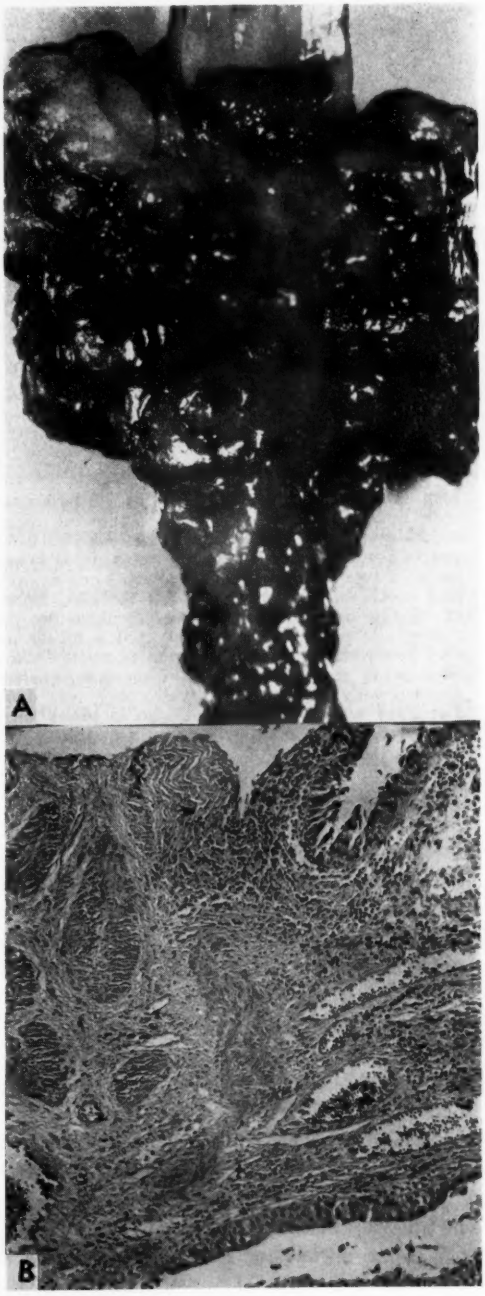



Fig. 12.—*A*, close-up of portion of original specimen (which included kidney, ureter, and cuff of bladder), showing tumor in lower part of ureter and cuff of bladder. *B*, histologic section, same tumor, showing papillary carcinoma, Grade 2, no infiltration. × 100. Patient was a 65-year-old white man who was first hospitalized elsewhere because of hematuria in 1948, at which time two or more papillary tumors ("papillary carcinoma, Grade 2") of the bladder were excised suprapubically and fulgurated. At that time left hydronephrosis was present. He had no further symptoms until January 1953, when he again had gross hematuria. Urogram showed hydronephrosis and hydroureter, and cystoscopic study showed papillary bladder tumor, which was resected transurethrally (papillary carcinoma, Grade 2). Diagnosis of primary ureteral carcinoma not made until April 1955, when hematuria recurred and tumor appeared at ureteral orifice, as well as a papillary tumor near vesical orifice. Nephroureterectomy with partial cystectomy (2 stages) was

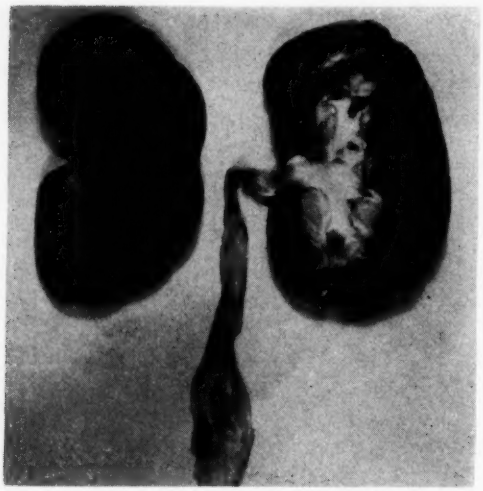


Fig. 13.—Gross specimen including only kidney with upper two-thirds of ureter, showing small papillary tumor in mid-ureter. Patient was a 60-year-old white woman admitted with gross hematuria of two months' duration, with some dysuria and nocturia. Cystoscopic study revealed spurts of bloody urine from right ureteral orifice. A retrograde pyelogram demonstrated a filling defect in mid-ureter, but dilatation of ureter below this point was also noted. Two-stage nephroureterectomy with partial cystectomy was done. Papillary tumor was present also in lower third of ureter. Histologically this was a papillary carcinoma, Grade 2, with superficial but not deep infiltration. Patient alive and well for four years.

followed for more than four years. Whitlock, McDonald and Cook, in studying 19 patients with carcinoma of the ureter five years or more after the operation, noted that 10 (66.7 per cent) of the patients with papillary tumor, 7 (14.3 per cent) of those with papillary and infiltrating tumor, and none of those with nonpapillary infiltrating tumors were surviving at the end of five years.

Recently, Cook and his associates reported a follow-up of the 220 patients with tumors of the ureter and pelvis studied at the Mayo Clinic between 1910 and 1954. Of those surviving five years, he found that 66 per cent had noninfiltrating tumors; only 1 patient with an infiltrating carcinoma lived three years or more. Of 23 patients of this series with squamous cell carcinoma of the renal pelvis all were dead within five years except 1 who lived six and one-half years. In our series no patients with squamous cell carcinoma of the renal pelvis survived more than three years.

We also encountered some difficulties with the follow-up of these patients and unfortunately were unable to locate several of the old histories or to find the patient.

The survival rate in our series of carcinoma of the pelvis and ureter is noted in Tables 13 and 14 respectively.

In general, survival is directly related to the degree of infiltration and to the histologic type of the tumor. It is notable that 1 patient with an infiltrating Grade IV carcinoma of the ureter survived eleven years and died of coronary thrombosis without evidence of metastasis.

It seems that better survival of patients with the infiltrating type of carcinoma will depend upon increased awareness, with early diagnosis and treatment.

## SUMMARY

Observations on 19 patients with pelvic tumors and 16 patients with ureteral tumors are made. Of the pelvic tumors, 78.9 per cent occurred in the male, 21 per cent in the female; 75 per cent of the ureteral tumors occurred in the male and 25 per cent in the female. Of the pelvic tumors, 36.8 per cent were multiple, as were 68.7 per cent of the ureteral tumors; 65 per cent had gross hematuria as a presenting complaint, lumbar or abdominal pain being less common. Of the patients with ureteral tumor, 37.5 per cent actually had tumor protruding from the ureteral orifice. The majority of the patients had significant roentgenographic signs. Of the 16 ureteral tumors, 6 were of the papillary variety, 7 of the papillary infiltrating type and 3 of the infiltrating

type. Of the 19 pelvic tumors, 5 were papillary, 6 papillary and infiltrating, 6 infiltrating, 1 mucoid adenocarcinoma and 1 papillary adenocarcinoma. The survivals are correlated with the type of carcinoma.

## CONCLUSIONS

The majority of patients with carcinoma of the renal pelvis or ureter present significant and usually diagnostic symptoms and clinical signs. The diagnosis must be based upon a careful evaluation of the patient's complaints and the cystoscopic and roentgenographic data. It should be especially considered in the case of a patient with a history of hematuria and/or lumbar pain, the presence of a filling defect on the urogram or retrograde pyeloureterogram, decreased unilateral renal function, hydronephrosis, hydroureter and, cystoscopically, the presence of unilateral hematuria, vesical tumor, and/or a dilated or congested ureteral orifice.

Nephroureterectomy with excision of a cuff of the bladder is recommended for all patients. Conservative operation is indicated only for those patients in whose cases the preservation of renal function is imperative.

There is a definite need for more careful pathologic study and prolonged follow-up investigations.

The careful work of McDonald and his collaborators, and Whitlock and his associates demonstrated the value of careful histologic evaluation in relation to the ultimate prognosis. The authors realize that the series here presented is relatively small and that the patients have not been followed for a sufficient time in all cases for conclusions to be reached. In general, however, survival has been directly related to the histologic picture.

**Authors' Note:** We are indeed grateful to Drs. David M. Davis, Walter W. Baker and Willard M. Drake for their kind permission to include their private patients in this study.

We should like also to thank Dr. Paul H. Jernstrom, Associate Director of Clinical Laboratories, Jefferson Hospital, for his assistance in reviewing the pathologic material.

## SCHLUSSFOLGERUNGEN

Die Mehrzahl der Kranken mit einem Krebs des Nierenbeckens oder des Harnleiters bietet charakteristische und gewöhnlich diagnostische Symptome und klinische Krankheitszeichen. Die Diagnose muss sich auf eine sorgfältige Auswertung der Beschwerden des Kranken und auf die zystoskopischen und röngenographischen Befunde stützen und sollte besonders dann in Betracht gezogen werden, wenn in der Krankheitsgeschichte Blut im Harn oder Schmerzen in der Lendengegend oder beides angegeben wird, wenn das intravenöse oder retrograde Urogramm einen Füllungsdefekt im Nierenbecken oder im Harnleiter zeigt, wenn eine einseitige Herabsetzung der Nierenfunktion, eine Hydronephrose oder ein Hydroureter besteht und wenn die Zystoskopie das Vorliegen einer einseitigen Harnblutung, einer Blasengeschwulst oder einer erweiterten oder gestauten Harnleiteröffnung nachweist.

In allen Fällen wird eine Resektion der Niere und des Harnleiters mit Ausschnitt einer Harnblasenstulpe empfohlen. Eine konservative Operation ist nur bei Kranken angezeigt, bei denen die Erhaltung der Nierenfunktion unerlässlich ist.

Es ist dringend notwendig, auf sorgfältigeren pathologischen Untersuchungen und auf lange ausgedehnten Nachuntersuchungen des Kranken zu bestehen.

Die sorgfältigen Arbeiten McDonalds und seiner Mitarbeiter und Whitlocks und seiner Assistenten haben den Wert genauer histologischer Auswertung für die Beurteilung der endgültigen Prognose dargelegt. Die Verfasser sind sich bewusst, dass das von ihnen hier vorgestellte Krankenmaterial verhältnismässig klein ist,

und dass nicht alle ihre Patienten genügend lange nachuntersucht worden sind, um Schlussfolgerungen zu gestatten. Im allgemeinen aber lässt sich die Überlebensdauer in direkte Beziehung zum histologischen Bilde bringen.


RESUMEN

La mayor parte de los enfermos con carcinoma de la pelvis renal o del ureter presentan síntomas, diagnósticos y signos clínicos careterísticos. El diagnóstico debe basarse en la evaluación de la molestias que aqueja el enfermo y en los datos cistoscópicos y radiológicos. En el caso de un enfermo con historia de hematuria o del dolor lumbar deben ser especialmente considerados los defectos de repleción en el urograma o en el pieloureterograma retrógrado, la función renal unilateral disminuida, la hidronefrosis, el hidroureter y, cistoscopicamente, la hematuria unilateral, el tumor vesical y el orificio ureteral dilatado o congestionado.

En todos los casos está indicada la nefroureterectomía comprendiendo un rodete vesical. Solamente estará indicado el tratamiento conservador en los enfermos en que sea ineludible preservar la función renal.

Es absolutamente necesario llevar a cabo estudios anatomopatológicos más minuciosos, así como seguir por mucho tiempo el curso de los operados.

Los cuidadosos trabajos de McDonald y sis colaboradores, así como los de Whitlock y los suyos han demostrado la importancia de la evaluación histopatológica afinada en relación con el pronóstico definitivo. Los autores reconocen que estas estadísticas suyas son relativamente pequeñas y que los operados no han sido seguidos ulteriormente tiempo suficiente para poder sacar conclusiones. Por lo general la supervivencia está en íntima relación con el cuadro histopatológico.



CONCLUSIONS

La majorité des malades atteints de carcinome du bassinet ou de l'uretère présentent des symptômes et des signes cliniques nets. Le diagnostic doit être pasé sur les données cystoscopiques et radiologiques et sur l'étude approfondie des symptômes, tels que: hématurie, douleurs lombaires, défaut de remplissage (urogramme ou pyélo-urétérogramme), diminution unilatérale de la fonction rénale, hydronéphrose, hydro-uretère, présence à la cystoscopie d'une hématurie, d'une tumeur vésicale, d'un orifice urétéral dilaté ou congestionné.

La néphro-urétérectomie, avec excision d'un segment de vessie, est recommandée dans tous les cas. L'opération conservatrice n'est indiquée que chez les malades où il est indispensable de préserver la fonction rénale.

Il est nécessaire de faire une étude pathologique approfondie et de pratiquer des examens répétés minutieux.

Les travaux de McDonald et ceux de Whitlock et de leurs collaborateurs, démontrent la valeur d'une évaluation histologique poussée en veu du pronostic. Les auteurs sont conscients du fait que la série de cas ici présentée est relativement minime et que les malades n'ont pas toujours été suivis pendant assez longtemps pour aboutir à des conclusions. En général cependant, la survie a été en rapport direct avec le tableau histologique.



RIASSUNTO

Nella maggioranza dei casi i pazienti affetti da carcinoma della pelvi o dell'uretere presentano sintomi caratteristici.

La diagnosi può fondarsi sull'accurata interpretazione dei disturbi rifeniti dal paziente, sui dati cistoscopici e su quelli radiologici. Si deve dare importanza, quando vi è una storia di ematuria e di dolori lombari, alla presenza di difetti di riempi-

mento dimostrati dalla urografia e dalla pielografia ascendente, alla diminuzione della funzione renale monolaterale, all'idronefrosi, alla dilatazione ureterale e ad alcuni dati rilevati mediante cistoscopia (ematuria monolaterale, tumore vescicale, dilatazione o congestione del meato ureterale).

L'intervento di scelta è rappresntato dalla nefro-ureterectomia con asportazione di una porzione della vescica. La cura conservativa và riservata soltanto a quei pazienti in cui è assolutamente necessaria la conservazione della funzione del rene.

Si sente senz'altro il bisogno di studi anatomo-patologici più accurati e di controlli a distanza molto prolungati nel tempo.

Gli accurati studi di McDonald e collaboratori e di Whitlock e collaboratori dimostra infatti chiaramente l'importanza di una precisa diagnosi istologica ai fini della valutazione prognostica. Stando a quanto sopra, gli autori si rendono conto che il numero dei pazienti presentati in questo lavoro è piuttosto ridotto, e i risultati a distanza seguiti per troppo breve tempo da poter trarre conclusioni di carattere generale; in generale, però, le quote di sopravvivenza sono in relazione diretta al quadro istologico.

## BIBLIOGRAPHY


Ackerman, L. V.: Mucinous Adenocarcinoma of the Pelvis of the Kidney, J. Urol. 55:36-45, 1946.

Arcadi, J. A.: Mucus-Producing Cystadenocarcinoma of the Renal Pelvis and Ureter, Arch. Path. 61:264-268, 1956.

Baker, W. J., and Graf. E. C.: Tumors of the Ureter, J. Urol. 70:390-409, 1953.

Bothe, A. E.: Carcinoma of the Renal Pelvis and Ureters, J. Urol. 49:69-76, 1943.

Bothe, A. E.: Relationship of Epithelial Buds to Carcinoma of Pelvis of the Kidney, Ureter and Bladder, J. Urol. 53:451, 1945.

Brodny, M. L., and LeVine, B. E.: Hazards in Diagnosis of Tumors of the Renal Pelvis, J. Internat. Coll. Surgeons 20:161-165, 1953.

Buford, C. E.; Glenn, J. E., and Buford, E. H.: Primary Carcinoma of the Ureter, With Report of Two Cases, J. Urol. 60:337-344, 1948.

Carson, W. J.: Metastatic Carcinoma in Ureter: Report of Additional Case, Ann. Surg. 86:549-555, 1927.

Colston, J. A.; Campbell, and Arcadi, J. A.: Bilateral Renal Papillomas; Trans-Pelvic Electro-Resection with Preservation of Kidney; Contralateral Nephrectomy; Four Year Survival, Cook, E. N., and Counseller, V. S.: Primary Epithelioma of the Ureter, J.A.M.A. 116:122-127, 1941.

Cook, E. N.; Culp, O. S.; McDonald, J. R., and Utz, D. C.: Carcinoma of the Renal Pelvis and Ureter. Paper presented June 5, 1957 at meeting of the A.M.A. Section on Urology, New York, N. Y.

Counseller, V. S.; Cook, E. N., and Seefeld, P. H.: Primary Epithelioma of the Ureter: A Follow-Up Study of Eighteen Cases with the Addition of Nine Cases, J. Urol. 51:606-615, 1944.

Creecy, A. A.: Carcinoma of the Ureter, J. Urol. 68:591-602, 1952.

Dees, J. E.: Prognosis of Primary Tumors of Renal Pelvis and Ureter, J. Urol. 75:419-423, 1956.

Drexler, L. S.: Metastatic Carcinoma of Ureter in Carcinoma of Cervix. Am. J. Obst. & Gynec. 57:391-395, 1949.

Everett, H. S., and Wayburn, G. J.: Unique Case of Submucosal Epithelial Nests in Ureter and Renal Pelvis, J. Urol. 56:310, 1946.

Fagerstrom, D. P.: Proliferative Tumors of the Ureter and Renal Pelvis, with Further Observations on the Significance of Epithelial Cell Nests, J. Urol. 59:333-357, 1948.

Ferris, D. O., and Dant, R. V.: Epithelioma of Pelvis of Solitary Kidney Treated by Electrocoagulation, J. Urol. 59:577, 1948.

Foord, A. G., and Ferrier, P. A.: Primary Carcinoma of the Ureter. J.A.M.A. 112:596-601, 1939.

Foot, N. C.; Humphreys, G. A., and Whitmore, W. F.: Renal Tumors, J. Urol. 66:190, 1951.

Gahagan, H. Q., and Reid, W. K.: Squamous Cell Carcinoma of the Renal Pelvis: Three Case Reports and Review of the Literature, J. Urol. 62: 139-151, 1949.

Harrison, F. G.; Warren, H. L., and Fust, J. A.: Primary Carcinoma of the Ureter, Ann. Surg. 130: 902, 1950.

Henriksen, E.: The Lymphatic Spread of Carcinoma of the Cervix and of the Body of the Uterus, Am. J. Obst. & Gynec. 58:924-940, 1949.

Herbut, P. A.: Urological Pathology. Philadelphia: Lea & Febiger, 1952, Vol. 1, pp. 426-430.

Jacob, N. H. Jr., and Mau, W.: Metaplasia of Ureteral Epithelium Resulting in Interstitial Mucosa and Adenocarcinomatous Transformation; Report of Two Cases, J. Urol. 65:20-24, 1951.

Jaffe, S. A., and Mendillo, A. J.: Primary Carcinoma of the Ureter. Am. J. Surg. 62:126-133, 1943.

Keen, M. R.: Primary Ureteral Tumors, J. Urol. 69:231-242, 1953.

Kimball, F. N., and Ferris, H. W.: Papillomatous Tumor of the Renal Pelvis Associated with Similar Tumors of the Ureter and Bladder, J. Urol. 31:257-304, 1934.

Kirshbaum, J. D.: Metastatic Tumors of Ureters, J. Urol. 30:665-677, 1933.

Kittredge, W. E.; Henthorne, J. C., and Whitehead, J.: Glandular Metaplastic Malignancy in the Urinary Tract, J. Urol. 58:228-288, 1947.

Lazarus, J. A.: Primary Tumors of the Ureter,

with Special Reference to the Malignant Tumors: Report of Three Cases, Ann. Surg. 99:769-795, 1934.

Lazarus, J. A., and Marks, M. S.: Primary Carcinoma of the Ureter with Special Reference to Hydronephrosis, J. Urol. 54:140-157, 1945.

McDonald, J. R., and Priestley, J. T.: Carcinoma of Renal Pelvis: Histopathologic Study of Seventy-Five Cases with Special Reference to Prognosis, J. Urol. 51:245-258, 1944.

Maclean, J. T., and Fowler, V. B.: Pathology of Tumors of the Renal Pelvis and Ureter, J. Urol. 75:384-415, 1956.

Melicow, M. J.: Tumors of the Urinary Drainage Tract, J. Urol. 54:186-193, 1945.

Mirabile, C. S., and Spillane, R. J.: Metastatic Adenocarcinoma of the Ureter with Obstruction: Case Report, J. Urol. 70:187-190, 1953.

O'Conor, V. J., and Greenhill, J. P.: Endometriosis of Bladder and Ureter, Surg., Gynec., & Obst. 80:113-119, 1945.

O'Conor, V. J.: The Treatment and Prognosis of Papillary Tumors of the Renal Pelvis and Ureter, J. Urol. 61:488, 1949. The Diagnosis of Tumors of the Renal Pelvis and Ureter, J. Urol. 75:416-418, 1956.

Plaut, A.: Diffuses dickdarmahnliches Adenom des Nierenbeckens mit geschwulslartiger Wucherung von Gefassmuskulatur. Ztschr. f. urol. Chir. 26:362-578, 1929.

Presman, D., and Ehrlich, L.: Metastatic Tumors of the Ureter, J. Urol. 59:312-325, 1948.

Ragins, A. B., and Rolnick, H. C.: Mucus Producing Adenocarcinoma of the Renal Pelvis, J. Urol. 63:66-73, 1950.

Randall, A.: Endometrioma of Ureter, J. Urol. 46:419-426, 1941.

Renner, M. J.: Primary Malignant Tumors of Ureter, Surg. Gynec. & Obst. 52:793-803, 1931.

Scott, W. W.: Primary Carcinoma of Ureter, Surg., Gynec. & Obst. 58:215-217, 1934. Review of Primary Carcinoma of Ureter: Presenting Two Cases, J. Urol. 50:45-64, 1943.

Scott, W. W., and Boyd, H. L.: A Study of the Carcinogenic Effect of Betalnaphthylamine on the Normal and Substituted Isolated Sigmoid Loop Bladder of Dogs, J. Urol. 70:914-925, 1953.

Scott, W. W.: Tumors of the Ureter. In Campbell, M.: Urology. Philadelphia & London: The W. B. Saunders Company, 1954, section 10, pp. 1021-1041.

Senger, F. L., and Furey, C. A.: Primary Ureteral Tumors, with a Review of the Literature Since 1943, J. Urol. 69:243, 1953.

Taylor, J. A.: Primary Carcinoma of the Ureter, J. Urol. 65:797-804, 1951.

Twinem, F. P.: Primary Tumors of the Ureter, J.A.M.A. 163:808, 1957.

Whitlock, G. F.; McDonald, J. R., and Cook, E. N.: Primary Carcinoma of the Ureter: A Pathologic and Prognostic Study, J. Urol. 73:245, 1955.

Wishard, W. N. Jr.: Primary Carcinoma of the Ureter, J. Urol. 70:191-195, 1953.

Long before he was called to the royal bedside at Windsor Castle, Jenner had a very large practice, and in the wards of University College Hospital, no student ever forgot his terse dogmatic sentences and his mania for precision. His inspiration came to him from the sick patient on whose case he was lecturing, and not from the audience around him, and even though he had been kept late for his demonstration and the students had departed for lunch, he talked as well to a handful as to the whole class. He was never slack, or lenient, or vague. As he spoke slowly, from notes made on the backs of envelopes, the students could write down everything; facts, not cobwebs of theory, facts only, but once Jenner had spoken they were memorized for ever.

—*Williams*

# The Variant Renal and Suprarenal Blood Supply with Data on the Inferior Phrenic, Ureteral and Gonadal Arteries

## A Statistical Analysis Based on 185 Dissections and Review of the Literature

ROBERT J. MERKLIN, Ph.D., AND NICHOLAS A. MICHELS, Dr.Sc., F.I.C.S. (Anat.)

PHILADELPHIA, PENNSYLVANIA

A POINT rarely stressed in most textbooks of anatomy, surgery and even urology, is the intimate relation of the renal arteries to the suprarenal gland, and, vice versa, of the suprarenal arteries to the kidney, the vascular supply of the two organs in most instances being intimately intertwined. Frequently the renal artery gives off from 2 to 5 slender branches to the suprarenal gland, while inferior suprarenal arteries stemming from the aorta or the renal artery often supply from 1 to 4 small branches to the superior pole of the kidney and its fat body (capsular branches).

A second point, seldom emphasized, is the fact that constitutional differences in the arterial vascularization of the kidneys and suprarenal glands are as marked and frequent as are those of the liver and gallbladder, now more and more being appreciated and recognized. From the vast array of statistical data recorded in the literature on normal and aberrant renal arteries, the conclusion is warranted that the standard textbook description of the renal blood supply holds true only in about one-third of the population, while that of the liver is applicable in slightly over one-half of the subjects (Michels, 1955). In his pioneer, monumental classic work on the arteries of the suprarenal gland, comprising a dissection of 111 cadavers, Gérard of France (1913), concluded that the patterns of the suprarenal blood supply vary to such an extent that no two are ever alike.

More than that of any other organ in the body, the vascularization of the kidney ("viscus elegantissimum" of the ancient anatomists), has been the topic of repeated anatomic investigation, statistical analysis and description. The major and most significant contributions during the past seventy-five years are those of: Macalister (1883), Thomson (1891), Helm (1895), Brewer (1897), Brödel (1901), Kolster (1902), Young and Thompson (1903), Pohlman (1905), Ekehorn (1907-22), Albarran and Papin (1908), Broman (1908), Levi (1909), Seldowitsch (1909), Robinson (1909), Eisendrath and Strauss (1910), Gérard (1911-13), Jeidell (1911), Boetz (1912), Bonney (1912), Rupert (1913-15), Bremer (1915), Gillaspie, Miller, and Raskin (1916), Lipshutz and Hoffman (1918-26), Jeanneney and Massé (1920), Eisendrath (1920), Nanagas (1921), Petrén (1921), Smirnoff (1922), Poynter (1923), Golubev (1927), Santaelia (1927), Adachi (1928), Heidsieck

From the Daniel Baugh Institute of Anatomy of the Jefferson Medical College, Philadelphia. Aided by a grant from the American Philosophical Society.

Submitted for publication Aug. 14, 1957.

(1928), Hellström (1928), Lapeyre (1929), Hou-Jensen (1929), Dos Santos (1930), Taniguchi (1930), Fetter (1931), Westerborn (1931), Carson (1932), Lloyd (1935), Miyashita (1935), Anson and McVay (1936), Anson, Richardson and Minear (1936), Jewett (1939), Pick and Anson (1940), Weinstein, Countiss and Derbes (1940), Anson, Pick and Cauldwell (1942), Anson, Cauldwell, Pick and Beaton (1947-48), Ronstrom (1947), de Quevedo (1948), Balint and Palkovich (1952), Busch (1954), Edsman (1954), Melkonian (1954), Anson and Kurth (1955), Douville and Hollinshead (1955), Graves (1954-56) and Smithuis (1956).

For pioneer discoveries of the structure of the kidney and its intra-organic vascular arrangement, the reader is referred to the seldom cited, unmatched classic monograph of Hou-Jensen (1930), who devoted three chapters to historic aspects (Galen, Bertin, Bellini, etc.), and cited many passages in the original text, including Vesalius' concept of the kidney's "vasa emulgentia," of which an illustration is included. Extensive statistical data on the position of the kidneys and renal vessels in respect to vertebral levels are those of Nanagas (1921), Adachi (1928), Heidsieck (1928), Taniguchi (1931), Anson and McVay (1936), and Moody and Van Nuys (1940). The anthropologic aspect of renal vascularization was presented by

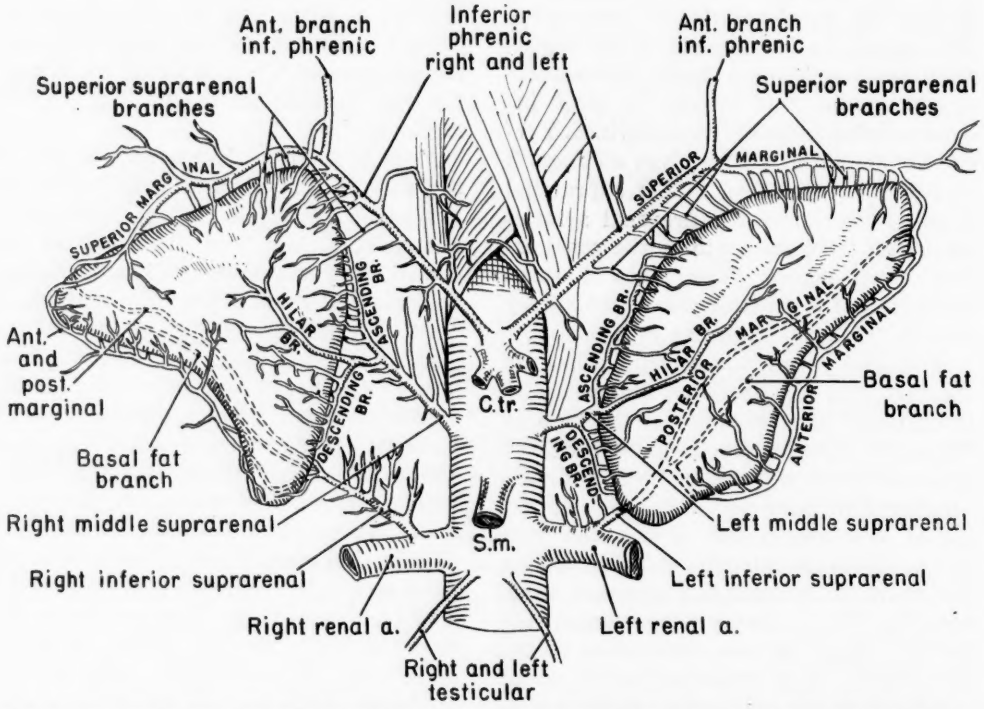



Fig. 1.—Composite drawing of the blood supply to the suprarenal gland (modified from Gérard, Fig. 1, 1913). General scheme of suprarenal arteries comprises: 1. Inferior suprarenals which have (a) slender collaterals, (b) terminals composed of marginals (anterior and posterior) and a basal fat branch. 2. Middle suprarenal, which has (a) slender collaterals and (b) terminals (ascending, descending, hilar, posterior). 3. Superior suprarenals derived from the phrenic trunk and its posterior division.

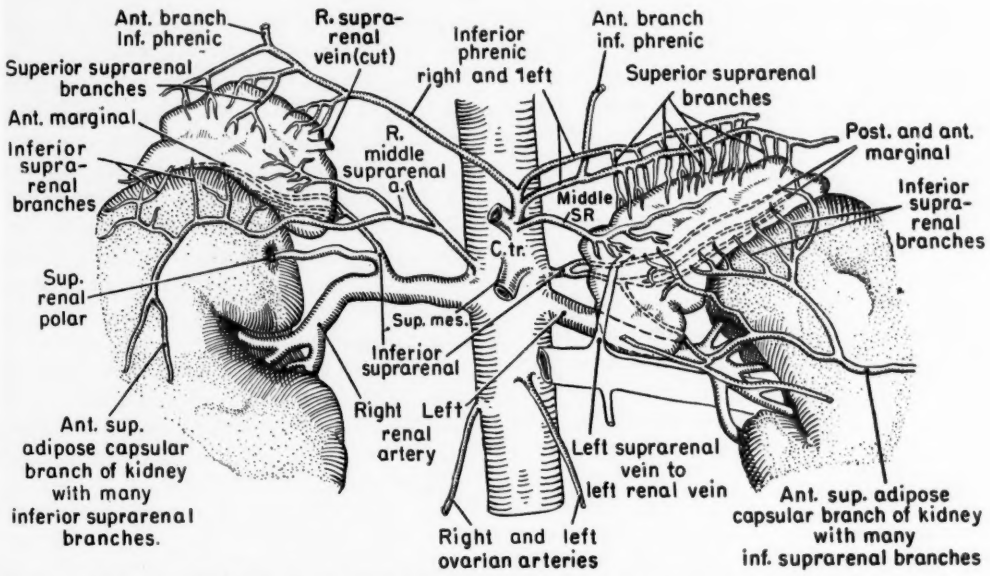

Ant. branch Inf. phrenic
R. supra-renal vein(cut)
Inferior phrenic right and left
Ant. branch inf. phrenic
Superior suprarenal branches
Ant. marginal
Inferior supra-renal branches
R. middle suprarenal a.
Superior suprarenal branches
Post. and ant. marginal
Middle SR
Inferior supra-renal branches
C. tr.
Sup. renal polar
Sup. mes.
Inferior suprarenal
Right Left renal artery
Ant. sup. adipose capsular branch of kidney with many inferior suprarenal branches.
Left suprarenal vein to left renal vein
Ant. sup. adipose capsular branch of kidney with many inf. suprarenal branches
Right and left ovarian arteries

Fig. 2.—Anterior superior adipose capsular branch of kidney (♀, 52 years, modified from Gerard, Fig. 15, 1913). On both sides, the adipose capsular branches give off numerous inferior suprarenal branches. On the right, the main suprarenal arises from a superior renal polar; on the left it stems from aorta, via a common trunk with adipose capsular branch. Right middle suprarenal stems from the aorta, via a common trunk with adipose capsular branch; left is from the celiac. Two left inferior phrenics supply numerous suprarenal branches.

Loth (1931) and Lloyd (1936). Investigations on the varied blood supply of the adrenal gland have been exceptionally few. None have matched the pioneer and classic contributions made by Levi (1909) and Gérard (1913). Articles worthy of note are those of Luna (1908), Adachi (1928), Pick and Anson (1940), Anson, Caldwell, Pick and Beaton (1947), Hollinshead (1952), Busch (1954) and Mazza (1954). The most extensive statistical reports on the inferior phrenics are those of Pick and Anson (1940), and Greig, Anson and Coleman (1951); others are those of Poynter (1923), Adachi (1928), Busch (1954) and Michels (1955).

A survey of the papers published on the renal and suprarenal blood supply shows that numerous and strikingly diverse methods have been employed in their description and classification. Percentage listings of the occurrence of aberrant (multiple) renal arteries are so astoundingly diversified, varying from 14 to 59 per cent (Poynter), as to be practically meaningless. There are many reasons for the contradictory reports. Some authors made their statistical analysis on the basis of bodies examined, while others considered only sides or the total number of kidneys examined. Many authors have published data on a single phase of vascularization, viz., the occurrence of renal polar arteries and their clinical significance in hydronephrosis. In the literature there is no unanimity as to what constitutes a supernumerary renal artery; such a vessel has been designated by different authors as abnormal, accessory, extrahilar, multiple, supernumerary or aberrant, leaving a statistical void as to their exact kind, number, site of origin and mode of

distribution. Few authors have considered the mode of terminal branching of the renal artery, and still fewer have given any information on the venous patterns.

To formulate and present a much-needed modern concept of the most salient varied patterns of the renal and suprarenal blood supply, as ascertained in a dissection of 185 kidneys and as evaluated from an extensive statistical analysis of the literature, is the primary purpose of this paper. Despite the baffling and tedious task, more than three years in duration, the statistical data in the literature (150 papers) were assembled in table form to a length never attempted before, thereby, at long last, giving a clear cut, overall concept of existent variational anatomic features met with in the blood supply of the kidney and suprarenal gland.

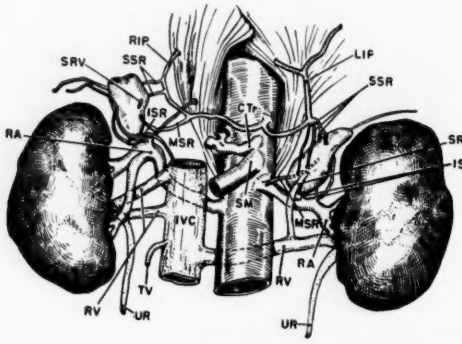



Fig. 3.—W ♂, 85 years. Typical pattern of renal and suprarenal blood supply. Right renal of the distributed type divides early into an anterior and posterior trunk, which subdivide at hilum into two branches. In Graves's terminology of the segmentation of the kidney applied to this specimen, the terminal branches of the right renal, purportedly, are, from above downward, the upper, middle, posterior and lower segmental branch. The apical branch to apical segment could not be seen, its origin being intrarenal. Left renal is of the magistral type, and deep in the hilum, divides into an upper, posterior and lower segmental branch. The other segmental branches (apical, middle) could not be seen in the hilum, their origin being inside the kidney. Inferior phrenics (*RIP, LIP*) arise from aorta, via a common trunk and supply the superior suprarenals (*SSR*). Right middle suprarenal (*MSR*) from phrenic, left from renal. Right and left inferior suprarenals (*ISR*) from renal, the right giving off a capsular branch. Note retroaortic course of left renal vein (*RV*).

Knowledge of the variational anatomic picture of the renal and suprarenal arteries is an essential part of the surgeon's knowledge, not only for nephrectomy, but in the diverse modern operative procedures that are being performed on the kidney, to wit: nephrotomy, nephrolithotomy, heminephrectomy, nephrostomy, pyelotomy, pyeloplasties and nephropexy, not to speak of the many corrective operations performed on dysfunctioning ureters. More and more, adequate knowledge of the varied patterns of the renal blood supply is needed for competence in diagnostic roentgen procedures, i.e., in reading and correctly interpreting roentgenographic records of a distorted pelvis and complex hilar arterial and venous patterns shown by excretion urographic (pyelographic study) and renal arteriographic (renal angiograms). The striking usefulness of the latter in the preoperative diagnosis of hydronephrosis has recently been demonstrated by Edsman of Sweden (1954), and Riches of England (1955). The latter has shown that with diodone (70 per cent), renal angiographic study is a safe procedure, that its technic can easily be mastered and that it is a valuable diagnostic aid in the investigation of space-occupying lesions of the kidney, of congenital anomalies and of any condition for which partial nephrectomy is contemplated (23 angiograms are reproduced). Knowledge of varied possible arterial patterns is helpful to those who work with retroperitoneal pneumography, i.e., the use of air or oxygen for visualization of the renal complex, especially the detection of a horseshoe kidney as recently shown by Fetter, Varano and Ayres (1956).

In the following account, an additional (supernumerary) renal artery will be regarded as comprising: (1) an additional, separate aortic renal vessel; (2) an aortic

superior polar vessel; (3) an aortic inferior polar vessel; (4) a renal superior polar vessel; (5) a renal inferior polar vessel, or (6) a renal vessel derived from some other source, such as the inferior suprarenal, inferior phrenic, testicular or common iliac artery. This terminology was strictly adhered to in the compilation of the statistical tables and in the description of our own observations.

*Materials and Methods.*—Because of the difficulty of making a complete dissection of the kidney and suprarenal glands *in situ*, these organs with their pertinent blood supply were removed *en bloc* from 50 adult cadavers (male and female, white and Negro) under dissection in our anatomic laboratories. Each specimen comprised a retroperitoneal region extending from the first sacral up to approximately the tenth thoracic level, thus including a portion of the diaphragm. In no instance, had the specific region previously been interfered with or dissected by students. After each specimen had been thoroughly dissected, a complete drawing was made of all blood vessels supplying the kidney and suprarenal gland. To augment the statistical data, the renal arteries were studied in 43 additional cadavers, 1 of which had but one kidney (nephrectomy), bringing the total number of kidneys examined to 185. The final illustrations were made by an artist, who used the dissection sketches as his guide.

## OBSERVATIONS

1. *The Inferior Phrenic Artery.*—In nearly one-half of 50 specimens (22), the left and right inferior phrenic artery sprang from a common trunk that stemmed either from the celiac axis (8 cases) or from the aorta (14 cases). The site of origin of the common trunk was displaced to the left side of the aorta in 8 cases, that of the celiac, in 1 case. Strikingly aberrant (Figs. 9 and 11) were the origins of the common trunk from the left dorsal surface of the aorta (2 cases) and from the aorta to the left and below the superior mesenteric (1 case).

In many cases the left and right inferior phrenic each had a separate origin. Variants comprised: (1) both inferior phrenics from the aorta (8 cases) or the celiac (8 cases); (2) right inferior phrenic from the aorta, left from the celiac (6 cases); (3) left inferior phrenic from the aorta, right from the celiac (4 cases); (4) right inferior phrenic from the aorta (2 cases), left either from the renal artery or absent. These observations, with similar data from other authors, are recorded in Table 1.

2. *The Suprarenal Glands.*—Contrary

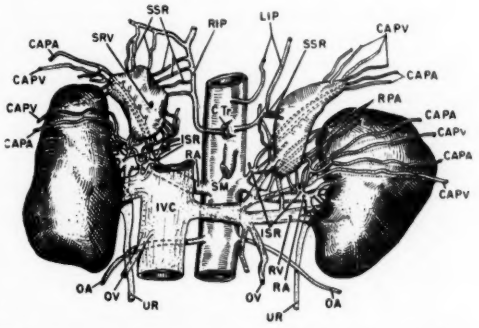



Fig. 4.—N. ♀, 65 years. Single renal arteries, both of the magistral type, showing late division (near hilum) into terminal branches. In accord with Graves's terminology of the segmentation of the kidney, branches of the right renal, purportedly, are from above downward, the apical, upper, posterior, middle and lower segmental branch. Left renal supplies in sequence, the apical, upper, posterior, middle and lower segmental branch. Inferior suprarenals (*ISR*), 3 in number, bilaterally, arise from various sections of the renal and supply superior renal polars, and adipose capsular branches (*CAPA*). Middle suprarenal is replaced, on right, by a branch from inferior suprarenal (*ISR*), on the left, by a branch from inferior phrenic. Superior suprarenals (*SSR*) are more numerous on right. Note entry and exit of arterial and venous capsular branches (*CAPS V*) from the suprarenal glands and the intimate relationship of the renal and suprarenal blood supply afforded through the inferior suprarenals (*ISR*) and their capsular branches.

TABLE 1.—*Origin of the Inferior Phrenic Arteries (in Order of Frequency)*

| | *Adachi* | *Caldwell and Anson* | *Greig, Anson and Coleman* | *Busch* | *Michels* | *Merklin and Michels* | *Total* | *Per Cent* |
|---|---|---|---|---|---|---|---|---|
| Separately from the celiac axis | 16 | 25 | 89 | 19 | 18 | 8 | 175 | 20.3 |
| Common trunk from the aorta | 11 | 27 | 77 | 14 | 24 (14L) | 14 (9L) | 167 | 19.7 |
| Right from aorta, left from celiac | 7 | 19 | 63 | 12 | 13 | 6 | 120 | 14.2 |
| Common trunk from celiac axis | 6 | 23 | 52 | 15 | 11 | 8 | 115 | 13.6 |
| Separately from the aorta | .... | 31 | 54 | 13 | 6 | 8 | 112 | 13.2 |
| Right from celiac, left from aorta | .... | 8 | 32 | 10 | 4 | 4 | 58 | 6.8 |
| Right from renal, left from aorta | .... | 5 | 17* | 6 | 3 | .... | 31 | 3.7 |
| Right from renal left from celiac | .... | 4 | 16 | 4 | 5 | 1 | 30 | 3.5 |
| Right from left gastric, left from left gastric | .... | .... | 6** | .... | .... | .... | 6 | 0.7 |
| Right from left gastric, left from aorta | .... | .... | 4 | .... | .... | .... | 4 | 0.5 |
| Right from aorta, left from renal | .... | 1 | 1 | 1 | .... | 1 | 4 | 0.5 |
| Right from celiac, left from left gastric | .... | 1 | 2 | .... | 1 | .... | 4 | 0.5 |
| Right from aorta, left from left gastric | .... | 1 | .... | .... | 2 | .... | 3 | 0.4 |
| Right from renal, left from renal | .... | .... | 3 | .... | .... | 7 | 3 | 0.4 |
| Other combinations | 2 | 1 | 9 | .... | 3 | .... | 16 | 1.9 |
| Total bodies | 42 | 146 | 425 | 94 | 90 | 51 | 848 | |

*In 4 of these the right vessel was from a superior aortic polar.
**In 3 bodies these arteries arose from a common trunk.
L = Origin from the left side of the aorta.

to standard textbook descriptions, these glands vary considerably in shape and size (Swinyard, 1940). They may be pyramidal, quadrilateral, foliate and occasionally spherical. The right suprarenal gland is usually quadrilateral, its inferior portion being somewhat thicker than the superior. The left suprarenal, in most instances, is leaf-shaped, the central vein constituting the stem of the leaf. Its lower portion is the thickest. Both right and left glands have a deep furrow or hilum at the exit of the central vein, that of the left being prominent.

The suprarenal glands investigated varied from 35 to 73 mm. in length, 15 to 40

mm. in width and 3 to 18 mm. in thickness. The average size of the left and the right suprarenal differed little; that of the left averaged 50 by 23 by 7 mm. and that of the right 50 by 27 by 6 mm. Topographically considered, the respective glands were located between the upper pole of the kidney and the abdominal portion of the aorta. The glands were enclosed in the renal fascia but were separated from the kidney by a pad of fat, and from the aorta not only by fat and connective tissue but also by the celiac ganglion. The right suprarenal gland was contiguous with the inferior vena cava, which crossed its ventral aspect. It was more closely confined by neighboring structures and at times extended over the superior pole of the kidney. Since the left suprarenal was invariably situated at the upper medial aspect of the kidney, a position often taken likewise by the right suprarenal, the glands can just as appropriately be called adrenal glands, as they often are.

The concept gained from many texts on anatomy that three unbranched, i.e., stem arteries supply each gland is obsolete and false. In Table 2 the arteries are classified according to the region of the gland they supply, viz., the superior, middle and inferior portions. The superior suprarenal arteries supply the superomedial, the middle suprarenal, the anteromedial aspect; the inferior suprarenal, the posterior and inferolateral aspect. Sites of origin of the superior suprarenals are grouped into those that arise from: (1) the inferior phrenic before its division into an anterior and posterior branch, (2) its posterior branch and (3) both sources.

The superior suprarenal arteries, as shown in Table 2, arose almost exclusively from the inferior phrenic. In 1 case the supply was directly from the aorta. In 4 cases the superior area of the left suprarenal gland received some blood directly from the aorta in addition to the supply coming from the inferior phrenic.

The middle suprarenal (usually single) had varied sites of origin, these being, on one side or the other as follows: the inferior phrenic (24 cases), the aorta (18 cases), the renal artery (4 cases) and the celiac axis (3 cases). Often the middle suprarenal was replaced, on one side or the other, by the superior (9 cases) or the inferior (41 cases) suprarenal artery. In 1 specimen with a middle suprarenal, the specific area was partially supplied by the inferior suprarenal.

The inferior suprarenal arteries are the most important, since they supply the thickest and largest part of the gland. They may be grouped into proximal, mid-

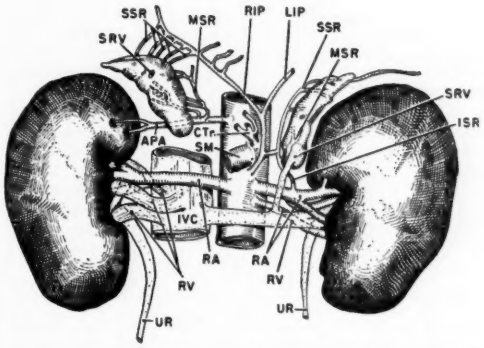



Fig. 5.—N ♂, 37 years. Sample of bilateral dual renal arteries. On the left, both are hilar; on the right, one is hilar with a precaval course, the other is a superior polar that bifurcates before entry. In the renal segmentation terms of Graves applied here, branches to the right kidney, purportedly, comprise the apical (2), upper, middle, posterior and lower segmental branch. In the left kidney, the upper renal, after giving off the posterior segmental gives rise to the apical, upper and middle segmental, while the lower artery becomes the lower segmental. Sample shows that an aortic superior polar may be considerably more than a renal artery, for here, it (*APA*) furnishes the main blood supply to the medial and inferior surfaces of the suprarenal gland (*MSR*). Inferior phrenics (*RIP, LIP*) arise via a common trunk from aorta below superior mesenteric and supply superior suprarenals (*SSR*). On the left, the inferior suprarenal (*ISR*), after its origin from renal, gives off the middle suprarenal (*MSR*) and anastomoses with the inferior phrenic.

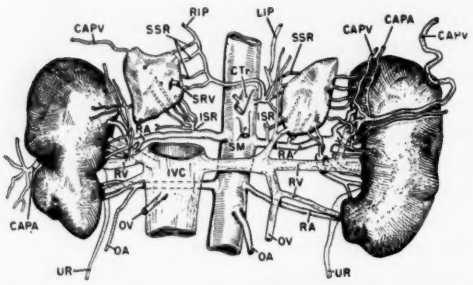



Fig. 6.—W ♀, 79 years. Bilateral dual renal arteries segmentally arranged and hilar in entry. Lower left renal could be mistaken for an inferior polar. Purportedly considered, it is the lower segmental branch of Graves. The upper left renal is of the distributed type and, following Graves terminology, supplies, in sequence, the apical, upper, posterior and middle segmental branch. Upper right renal, after giving off the posterior segmental, supplies the upper and middle segmental, and, via a superior suprarenal, gives off a slender polar (apical) branch. Lower right renal supplies the lower segmental branch, which, here, divides into its anterior and posterior branch outside of the kidney, such division, usually, being intrarenal (Graves). Superior suprarenals (*SSR*) stem from the phrenics (*RIP, LIP*), which arise from left side of aorta, via a common trunk. Inferior suprarenals (*ISR*) arise variously from upper renals, there being 3 main stems on the left, and one, on the right. Note copious blood supply to lateral surface of left suprarenal, furnished by rami from capsular adipose branches (*CAPA*), one of them passing through a hiatus in a tributary from capsule to renal vein. Note, also, emergence of capsular veins from right kidney and origin of right ovarian artery from renal, left from aorta.

dle and distal types, according to their point of origin from the renal artery. They are often multiple, but unlike the superior suprarenal arteries, they are larger and always branch before entering the gland. As is shown in Table 2, the inferior suprarenal blood supply came from the renal artery in 46 of 100 glands investigated. In 30 cases the supply was from the aorta, and in 17 cases both the aorta and the renal artery contributed to the supply of the posterior and inferolateral parts of the gland.

3. *The Kidneys.*—The average size of the left kidney was 9.8 by 5.2 by 3.3 cm.; that of the right kidney, 9.5 by 5.3 by 3 cm. Typically bean-shaped, the kidneys are often irregular in contour, one pole being smaller than the other or flattened to a varying degree. The pelvis faces medially; when it faces ventrally, vascular anomalies may be expected.

Within the renal fascia, the kidneys are covered with a thick pad of perirenal fat. A varying amount of fat (0.5 to 3 cm. thick, according to Iwanow, 1927) separates the suprarenal gland from the kidney, but no definite fascial layer was observed between the two glands as de-

TABLE 2.—*Origin of the Suprarenal Arteries (in 50 Dissections)*

| | *Superior* | | *Middle* | | *Inferior* | |
|---|---|---|---|---|---|---|
| | *Superomedial Part of Gland* | | *Anteromedial Part of Gland* | | *Posteroinferolateral Part of Gland* | |
| *From* | *Right* | *Left* | *Right* | *Left* | *Right* | *Left* |
| Inferior phrenic | 48½* | 47½ | 10 | 14 | 3 | 2 |
| Aorta | 1½ | 1½ | 8½ | 10 | 21 | 27 |
| Renal artery | .... | .... | 3 | 1 | 18P‡<br>18M<br>21D | 19P<br>13M<br>19D |
| Celiac axis | .... | .... | 1 | 2 | .... | 1 |
| Gonadal artery | .... | .... | .... | .... | .... | 2 |
| Replaced | .... | .... | 2S@<br>25½I | 7S<br>16I | .... | .... |

*Fractions denote specimens where designated area was supplied from more than one source.

‡ Level of origin from the renal artery. P = proximal; M = middle; D= distal.

@ S = replaced by superior suprarenal; I = replaced by inferior suprarenal.

| Source of Twiglets from Inferior Phrenic Artery | | |
|---|---|---|
| | Right | Left |
| Main stem | 29 | 39 |
| Anterior division | 4 | 4 |
| Both | 16 | 5 |

TABLE 3.—*The Arterial Supply of The Kidney*

| *Author (s)* | *Total Number of Kidneys* | *One Artery, Per Cent* | | *One Artery with an Upper Polar Branch* | *Two Arteries* | *One Hilar, 1 Upper Aortic Polar* | *One Hilar, 1 Lower Aortic Polar* | *One Artery with a Lower Polar Branch* | *Three Arteries* | *Two Arteries, 1 with an Upper Polar Branch* |
|---|---|---|---|---|---|---|---|---|---|---|
| Thane, 1882 (cited) | 200 | 174 | 87 | .... | .... | .... | .... | .... | 3 | .... |
| Thomson, 1891 | 419 | 320 | 77 | .... | .... | 29 | 17 | .... | .... | .... |
| Carlau, 1893 | 200 | 161 | 81 | .... | .... | .... | .... | .... | 1 | .... |
| Rousseau, 1894 (cited) | 100 | 77 | 77 | .... | .... | .... | .... | .... | .... | .... |
| Scmerber, 1895 (cited) | 200 | 155 | 78 | .... | 28 | 14 | 3 | .... | .... | .... |
| Helm, 1895 | 208 | 152 | 73 | .... | .... | .... | .... | .... | .... | .... |
| Brewer, 1897 | 302 | 217 | 72 | .... | 70 | .... | .... | .... | .... | .... |
| Kolster, 1902 | 206 | 152 | 74 | .... | 29 | .... | .... | .... | 3 | .... |
| Kubo, 1907 | 100 | 85 | 85 | .... | .... | .... | .... | .... | .... | .... |
| Albarran & Papin, 1908 | 63 | 49 | 77 | .... | 11 | .... | .... | .... | 3 | .... |
| Levi, 1909 | 192 | 143 | 75 | .... | .... | .... | .... | .... | .... | .... |
| Seldowitsch, 1909 | 300 | 247 | 82 | .... | 36 | 4 | 8 | 1 | 4 | .... |
| Iglesias, 1909 | 310 | 250 | 81 | .... | 14 | .... | .... | .... | .... | .... |
| Ancel, 1909 (cited) | 400 | 304 | 76 | .... | .... | .... | .... | .... | .... | .... |
| Eisendrath et al., 1910 | 200 | 146 | 73 | 25 | 16 | 5 | 8 | .... | .... | .... |
| Gérard, 1911 | 300 | 224 | 78 | .... | .... | .... | .... | .... | .... | .... |
| Bonney, 1912 | 118 | 95 | 85 | .... | .... | .... | .... | 7 | .... | .... |
| Rupert, 1913 | 100 | 57 | 57 | 13 | 15 | 4 | 2 | 5 | 3 | 1 |
| Rupert, 1915 | 216 | 129 | 60 | 12 | 30 | 7 | 6 | 1 | 5 | 10 |
| Gillaspie et al., 1916 | 66 | 30 | 46 | .... | .... | 5 | 8 | .... | .... | .... |
| Eisendrath, 1920 | 218 | 123 | 55 | 49 | .... | 13 | 31 | 2 | .... | .... |
| Smirnoff, 1922 | 660 | 495 | 75 | .... | .... | .... | .... | .... | .... | .... |
| Poynter, 1923 | 400 | 336 | 86 | .... | .... | .... | .... | .... | .... | .... |
| Iijima, 1925 (cited) | 60 | 45 | 75 | .... | .... | .... | .... | .... | .... | .... |
| Santaelia, 1927 | 200 | 160 | 80 | .... | 21 | .... | .... | .... | 4 | .... |
| Adachi, 1928 | 338 | 261 | 77 | .... | .... | .... | .... | .... | .... | .... |
| Hellström, 1928 | 200 | 113 | 57 | 41 | 22 | 14 | 5 | 1 | 4 | .... |
| Papin, 1928 | 320 | 238 | 74 | .... | .... | .... | .... | .... | .... | .... |
| Hou-Jensen, 1929 | 60 | 51 | 85 | .... | .... | .... | .... | .... | .... | .... |
| LaPeyre, 1929 | 70 | 56 | 80 | .... | 14 | .... | .... | .... | .... | .... |
| Dos Santos, 1930 | 93 | 66 | 71 | .... | .... | .... | .... | .... | .... | .... |
| Ribeiro, 1930 (cited) | 80 | 49 | 75 | .... | .... | .... | .... | .... | .... | .... |
| Fetter, 1931 | 168 | 94 | 56 | 24 | 11 | 8 | 21 | 2 | 2 | .... |
| Carson, 1932 | 869 | 537 | 62 | 91 | 82 | .... | .... | 18 | 25 | 23 |
| Lloyd, 1935 | 306 | 185 | 60 | 45 | 24 | 32 | 15 | 3 | 2 | .... |
| Miyashita, 1935 | 240 | 201 | 84 | .... | .... | .... | .... | .... | .... | .... |
| Anson et al., 1936 | 400 | 212 | 53 | .... | 44 | .... | .... | .... | 8 | .... |
| Pick & Anson, 1940 | 400 | 269 | 67 | .... | .... | .... | .... | .... | .... | .... |
| Weinstein et al., 1940 | 406 | 164 | 40 | 57 | 20 | 33 | 66 | 64 | 2 | .... |
| Ronstrom, 1947 | 200 | 134 | 67 | 24 | 10 | 18 | 8 | 6 | .... | .... |
| De Quevedo, 1948 | 106 | 83 | 80 | .... | .... | .... | .... | .... | .... | .... |
| Busch, 1954 | 200 | 159 | 80 | 14 | .... | 14 | 3 | .... | .... | .... |
| Edsman, 1954 | 388 | 325 | 86 | .... | .... | .... | 59 | 4 | .... | .... |
| Melkonian, 1954 | 200 | 156 | 78 | .... | 26 | .... | .... | .... | 4 | .... |
| Merklin & Michels, 1957 | 185 | 119 | 64 | 17 | 28 | 11 | 1 | 1 | 1 | 3 |
| TOTALS | 10,967 | 7,798 | 72 | 412 of 3,269 | 530 of 4,901 | 211 of 3,384 | 261 of 3,772 | 115 of 3,674 | 70 of 4,019 | 37 of 1,370 |

Standard Deviation of Percentages Listed 72% 2.51+—

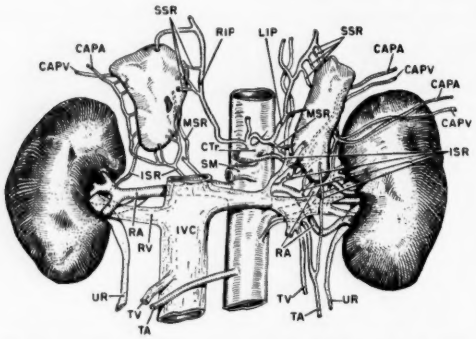



Fig. 7.—W ♂, 64 years. Single right and double left renals, latter crossing each other. Upper left renal enters caudal end of hilum and, in accord with the terms of Graves, purportedly, supplies the lower segmental branch. Lower renal, enters the cranial end of hilum and supplies the apical, upper, middle and posterior segmental branch. Right renal, after giving off the posterior segmental, supplies the apical, upper, middle and lower segmental branch. Superior suprarenals (*SSR*) from phrenics (*RIP, LIP*), are distributed to medial and superior surfaces of the suprarenal. Middle suprarenal (*MSR*), on right, from renal, on left, from phrenic. Inferior suprarenals (*ISR*) arise by 2 stem arteries from renal on right, and by 4 stem arteries, on the left, these being: 1 from celiac, 2 from renal and 1 from testicular artery (*TA*). On both sides, they give rise to adipose capsular branches (*CAPA*), that are accompanied by capsular veins. Note: an inferior suprarenal may cross in front of the left renal vein, as is often the case with the left gonadal artery.

scribed in some texts on anatomy. The fat does not enclose the suprarenal glands but is limited to their inferior surfaces. Fine vessels from the kidney and suprarenal gland entered the perirenal fat and, in many instances, veins emerging from the fat entered the suprarenal gland or joined the renal veins. Invariably, capsular (fat) branches arose from the suprarenal or the renal arteries. These varied in number (1 to 10) and in length, some of them extending the entire length of the kidney.

*Renal Arteries.*—The renal arteries from the aorta, when single, most often arose from its lateral aspect. The aortic level of origin of the right and left renal artery in the bodies investigated comprised the following variants: (1) same level for right and left renal (14 cases); (2) right renal higher than left (22 cases), and (3) left renal higher than right (11 cases). Single hilar renal arteries were present bilaterally in 35 cadavers, and, of these, 23 had no other branches, while 12 had either aortic or renal polar arteries.

Supernumerary (multiple) renal arteries comprised two types, hilar and polar. Polar arteries arose directly from the aorta or as branches of the renal hilar. Of 185 adult kidneys in which the arterial pattern was investigated, 34 had two renal hilar arteries; in 3 of these the arteries were crossed; there were additional branches in 5 (Table 4).

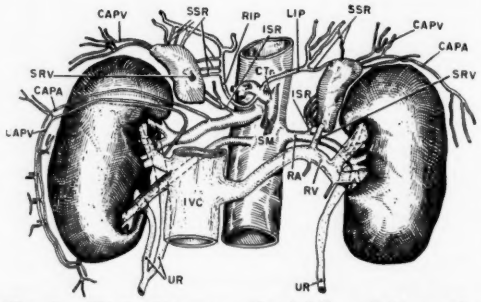



Fig. 8.—W ♀, 65 years. Dual hilar right renals with aberrant origin from anterior surface of aorta. Single left renal. In accord with the renal segmental terms of Graves, the upper right renal, purportedly, divides into an apical, upper, middle and posterior segmental branch. Lower right renal supplies the lower segmental branch which divides into its anterior and posterior branch before entry. Left renal, after giving off the posterior segmental, supplies the apical, middle and lower segmental branch. Superior suprarenals (*SSR*) from inferior phrenics (*RIP, LIP*), which have a separate origin from celiac. Middle suprarenal replaced by inferior suprarenal (*ISR*), that, bilaterally, arise from the renal. On right, note perirenal arterial half circle formed by an adipose capsular branch derived from the renal. The numerous terminals thereof, end in the subperitoneal plexus of Sir William Turner, and could thereby effect a renal collateral circulation, of which very little is known, anatomically considered. Capsular branches emerge directly from suprarenal glands, accompanied by veins (*CAPV*).

TABLE 4.—*Blood Supply of the Kidneys*

*1. Number of Arteries in 185 Kidneys*

| | | |
|---|---|---|
| 1 hilar | 119 | 64.3% |
| 2 hilar | 28 | 15.1% |
| 1 hilar with a polar branch* | 18 | 10.3% |
| 1 hilar; 1 aortic polar* | 12 | 6.5% |
| 2 hilar, from 1 a polar branch | 3 | 1.8% |
| 1 hilar with a polar branch; 1 aortic polar | 2 | 1.1% |
| 3 hilar | 1 | 0.5% |
| 2 hilar, from one a polar branch*; 1 aortic polar | 1 | 0.5% |
| 2 hilar; 1 aortic polar | 1 | 0.5% |

*One inferior polar in each instance.

*2. Branching of the Renal Artery*

| | | |
|---|---|---|
| UMLP** | 99 | 53.5% |
| U—LP | 39 | 21.1% |
| UML— | 18 | 10.3% |
| UM—P | 4 | 2.2% |
| MLP— | 3 | 1.8% |
| 2-3 branches missing or pattern altered | 22 | 11.9% |

The second hilar replaced the inferior branch in 24 of 34 specimens.

*3. Number of Veins in 185 Kidneys*

| | | | |
|---|---|---|---|
| Right side | One | 73 | 79.3% |
| | Two | 15 | 16.3% |
| | Three | 3 | 3.3% |
| | Four | 1 | 1.1% |
| Left side | One | 90 | 96.9% |
| | Two | 3 | 3.1% |

*4. Branching of the Renal Vein*

| | | |
|---|---|---|
| ML** | 97 | 52.4% |
| M | 22 | 11.9% |
| UML | 17 | 10.9% |
| L | 12 | 6.5% |
| UM | 10 | 5.4% |
| Other | 27 | 14.6% |

**U = upper, M = middle, L = lower, P = posterior } segmental branch

In 18 cadavers there was one hilar branch on one side, and 2 on the other, while in 7 there were double hilar branches to both kidneys. In 1 cadaver the left kidney had 2 hilar arteries and the right had 3 such arteries. Of the 16 kidneys with polar arteries derived from the aorta, 14 showed the polar artery entering the superior pole, and in 25 all but one of the polar branches derived from the renal artery entered the superior pole. Other variants comprised cases of (1) a single hilar branch, plus an aortic and renal polar branch (2 kidneys); (2) one hilar artery and 2 renal polar arteries (5 kidneys); (3) 2 hilar arteries with 2 renal polar and 1 aortic polar branch (1 kidney).

Terminal division of the renal artery into an anterior and a posterior branch occurred in all instances (185 kidneys), usually, being effected 3 to 5 cm. from the hilum. In 99 of 185 kidneys the anterior branch became subdivided into an upper,

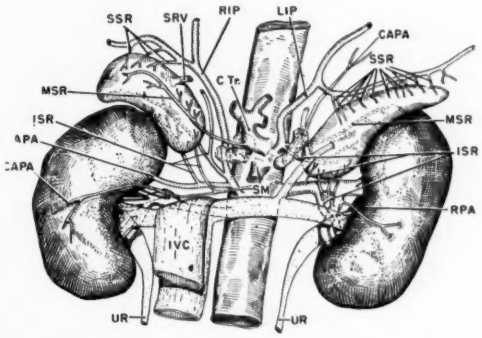



Fig. 9.—N ♂, 60 years. Strikingly aberrant origin of the blood supply to right side of diaphragm, most of right suprarenal, and to upper pole of kidney from an inferior phrenic (*RIP*) derived from aorta, at a renal level. In instances, this kind of an inferior phrenic arises from the renal trunk itself, and severance thereof, in nephrectomy, would result in complete necrosis of the suprarenal gland. Following Graves' terminology, the right renal, after giving off the posterior segmental, purportedly gives rise to the upper, middle and lower segmental branch, the latter subdividing into 3 rami. Left renal, after giving off the posterior segmental (with a middle segmental branch), gives rise to the apical, upper and lower segmental branch. Superior suprarenals (*SSR*) from separate phrenics, are very numerous on left, sparse on right. Right middle suprarenal (*MSR*) stems from celiac, left from inferior phrenic, the arteries passing through the celiac ganglion which they supply. Inferior suprarenals (*ISR*), on right, stem from 3 sources (superior polar, phrenic and an aortic capsular branch); on left, they arise from renal and its branches.

a middle and a lower branch, while the posterior branch continued without division and entered the hilum dorsal and superior to the pelvis. Polar arteries from either the renal artery or the aorta were always considered separate vessels, for despite their presence the prevailing pattern of branching of the renal artery was maintained in most instances. One or more branches of the typical divisional pattern of the renal artery were absent in 49 kidneys, the one most commonly absent being the middle branch (34 cases). The posterior branch was missing in 10 cases, the lower branch in 8 cases and the upper in 7 cases. The most striking aspect of the pattern of renal branching was the role played by the second hilar artery. In 24 of 34 specimens having such dual hilar arteries, the second hilar artery served as the lower kidney branch, and in a specimen with 3 hilar arteries 1 of them was the lower branch.

In contrast to the renal artery, the renal vein was usually single. Multiple veins occurred rarely on the left side (3 cases), being more frequent on the right (19 of

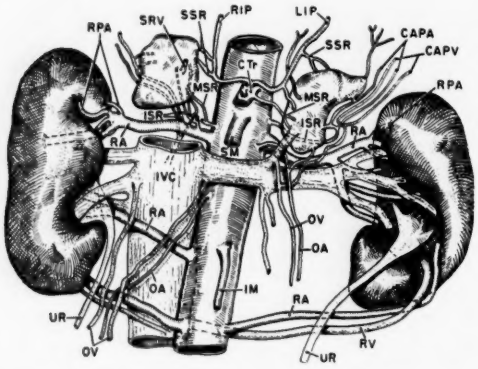



Fig. 10.—N ♀, 82 years. Three right and two left renal arteries, segmentally arranged, the lower 2 right being precaval in their course. Two right superior renal polars (*RPA*), one left. Lower right renal is an inferior polar (lower segmental); lower left, is a hilar artery, also a lower segmental. Both are accompanied by a vein. On right, the upper renal, in accord with Graves' terms, purportedly, gives rise to the apical (2), upper and middle segmental branch. Middle renal gives off the posterior segmental; the lower renal, the lower segmental branch. On left, the upper renal supplies the apical, upper (2), middle and posterior segmental, while the lower becomes the lower segmental. Superior suprarenals (*SSR*) from right and left phrenics (*RIP, LIP*). Right middle suprarenal (*MSR*) from aorta, left from celiac. Right inferior suprarenals (*ISR*) from renal, left from aorta and ovarian (*OV*). Arched ovarian artery and vein cross the left renal vein in the pedicle. Note ventral hilus of left kidney and adipose capsular branches (*CAPA*) from inferior suprarenal and from a tributary to ovarian vein.

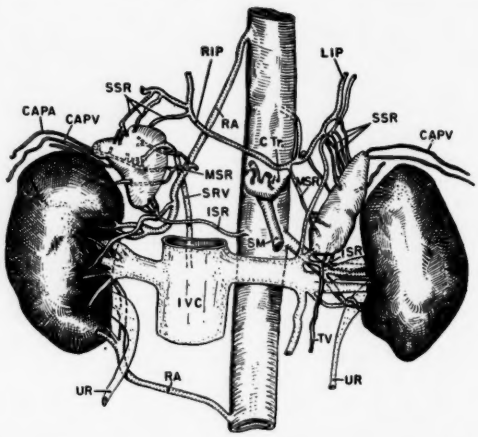



Fig. 11.—N. ♂, 60 years. Double hilar renals on right. Sites of their origin from aorta were widely separated (27 cm.), that of the upper was covered by the crus of diaphragm. Lower renal gives off an inferior polar (lower segmental). In Graves' terminology applied here, the upper right renal, purportedly, supplies, in sequence, a middle, apical, upper and posterior segmental branch. Left renal gives off the posterior and middle segmental, via a common trunk and the lower segmental. Right and left inferior phrenics (*RIP, LIP*) arise, via a common trunk, from dorsal aspect of aorta and give off superior suprarenals (*SSR*). Right middle suprarenal (*MSR*), from upper renal, gives off an adipose capsular branch (*CAPA*) and a slender upper polar. Left middle suprarenal replaced from left phrenic. Right inferior suprarenal (*ISR*) from aorta, left from renal. An adipose capsular vein (*CAPV*) emerges from left suprarenal gland. Right suprarenal vein (*SRV*) is exceptionally long before joining *IVC*. Left testicular vein (*TV*) is an exemplification of an arched gonadal vessel arching over the front of the renal vein in the renal pedicle, where it could be severed in a nephrectomy.

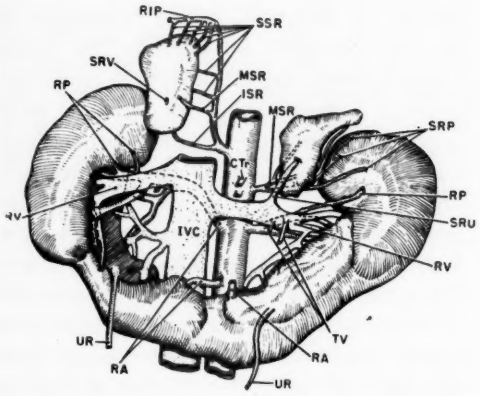



Fig. 12.—N. ♀, 36 years. Horseshoe kidney. This type, nearly invariably, has an aberrant blood supply. Here, there are dual right and triple left renals. The upper main renals arise at the same level and enter the hilum in a distributed manner. The lower two renals arise from aorta and unbranched, enter the isthmus of the fused kidneys. Evaluated in the segmental terms of Graves, the upper right renal, purportedly, gives off the apical (2), upper, middle and posterior segmental, the latter being a continuation of the posterior division of the renal. Left main renal supplies the upper, posterior and middle segmental, while the apical (polars) are derived from the middle suprarenals (*MSR*). Left middle suprarenal from aorta, right is replaced from inferior phrenic which furnishes the entire blood supply to the suprarenal gland. Left inferior phrenic was severed in removal of kidney.

92). The venous vessels of the kidney prevailingly had their exit at the inferior part of the hilum, the terminal branches of the arteries and veins being intermingled for a variable distance from the kidney. In nearly all instances, the veins were ventral to the aorta and renal arteries. A tributary to the renal vein from the dorsal aspect of the kidney, however, occurred frequently (30 per cent). Its retropelvic position is an important anatomic point to be remembered in surgical intervention on the kidney (Brödel).

To avoid needless repetition, the major observations made in our dissections are listed in tabular form and are discussed in the general summary.

## COMMENT AND CONCLUSIONS

On the basis of our own observations in the dissection of 185 adult kidneys and suprarenal glands, and from a comprehensive, thorough and analytic review of the literature, covering reports on approximately 11,000 kidneys, the variational anatomic picture of the blood supply of the kidney and suprarenal gland may be summarized as follows:

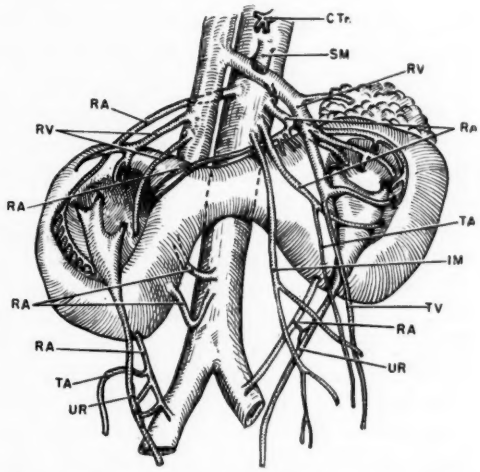



Fig. 13.—Man aged 71. Dumbbell or disc-shaped kidney with markedly aberrant blood supply, as usually the case. Seven renal arteries supply the fused kidneys. On right, 3 renals arise from aorta, one from common iliac. On left, there are 3 renals, lower from common iliac. In accord with the segmental terms of Graves, the upper right renal which is postcaval, purportedly, supplies, via a leash of vessels, the apical and upper segmental. The 3 renals arising near bifurcation point of aorta, supply the posterior and middle segmental, while the lower segmental is derived from the common iliac. On left, the upper renal supplies the apical, upper and posterior segmental. Middle renal gives off the middle segmental, while the renal from common iliac becomes the lower segmental. Note that the right kidney receives a branch from the upper left renal, the vessel crossing the aorta anteriorly. Blood supply to ureter from lower segmental branch. On left, note origin of testicular artery from middle aortic renal and its relation to the ureteropelvic junction. Right testicular from renal derived from common iliac. Site of origin of inferior mesenteric is above the isthmus, (Drawing modified after Herman and Fetterolf, Ann. Surg. June 1913).

Contrary to the usual antiquated textbook description, the suprarenal arteries are not represented by three stem arteries derived singly from the inferior phrenic artery, the aorta and the renal artery, but comprise for each gland, in every human body, an ever variable, large number of arteries (10 to 60), that encompass the suprarenal gland in an arterial circle. The latter is well anastomosed in the fetus and in young persons (Gérard), but in the adult it is reduced to slender anterior and posterior marginal branches, that are in relation with rami derived from the regional arteries supplying the gland (Figs. 1 and 2).

On the basis of their origin and distribution the suprarenal arteries may be classified into three groups, viz., the superior, middle and inferior. The superior suprarenals comprise from 3 to 30 twig-like branches, derived from the inferior phrenic. From 3 to 5 of these stem from its proximal portion, which courses medial to the gland; the remainder stem from its posterior division (after its bifurcation), which courses in concave fashion above the gland (Fig. 4). In some instances, all branches are derived from the posterior division of the inferior phrenic (Fig. 9). As slender rami and arranged in seriation, like the teeth of a comb, the superior suprarenals reach the medial and superior border of the gland, to be distributed to its anterior and posterior surfaces. Many of the arteries ramify superficially, or bifurcate before entering the parenchyma (Fig. 9); others anastomose with marginal branches. In some instances, some of the superior suprarenals arise directly from the aorta, celiac, superior polar or a second inferior phrenic (Figs. 2, 5 and 9).

The middle suprarenal may be regarded as the hilar artery. It is usually (85 per cent, Gérard) a single vessel and, predominantly, is distributed to the anteromedial surface of the gland, which it reaches by passing through or behind the celiac ganglion (Fig. 9). On the right side it invariably passes behind the inferior vena cava. Its terminals comprise an ascending and a descending medial marginal branch, a hilar branch, several posterior branches and, in many instances, an anterior superior adipose capsular branch to the kidney (Fig. 1). Most frequently, the middle suprarenal arises from the aorta, but in many instances, it takes origin from the proximal part of the inferior phrenic (Fig. 9), from the first part of the renal (Fig. 8) from an aortic superior polar (Fig. 5) or from the celiac trunk (Figs. 2 and 9). The artery is often double, in which case the accessory one may have any of the varied sites of origin previously listed. At times it is lacking, being replaced by a superior or inferior suprarenal (Fig. 4).

The inferior suprarenals are the most important, since they supply the thickest and largest part of the gland, entering the latter on its posterior and inferolateral surfaces. In about 66 per cent of subjects the inferior suprarenal is single (Gérard) and, predominantly, arises from the proximal part of the renal (Fig. 1), from one of its perihilar branches (Fig. 6) or from a superior polar renal (Fig. 5). Its terminals comprise anterior and posterior marginal branches and a basal fat branch distributed to the fat interposed between the kidney and the suprarenal gland (Fig. 1).

Aberrantly, the inferior suprarenal may arise from the aorta (Fig. 2), just above or below the origin of the renal (Fig. 4), from the middle or distal part of the renal (Fig. 8), from the lower of dual renals, from a superior polar renal (Fig. 4), from a trunk division of the renal (Fig. 9), from the testicular (ovarian, Figs. 7 and 10), from the inferior phrenic itself (Fig. 9)

or in a common trunk with the middle suprarenal from the aorta, renal or inferior phrenic (Fig. 9). Frequently (23 per cent according to Gérard), the inferior suprarenal is double, 1 arising from the aorta and the other from the renal near the hilus of the kidney, or from a superior aortic polar or one of its branches (Figs. 5, 6 and 7). In many cases multiple inferior suprarenals are present. These may spring from the varied sites of origin, as those listed for origin of the single type, and, they usually branch before entering the gland (Figs. 4, 6 and 7). Commonly, the anterior superior capsular adipose branch to the kidney, a collateral of the renal in most instances, gives off from 3 to 10 twigs to the inferior and lateral surface of the gland (Figs. 2 and 6). This branch may arise separately from the aorta, the middle suprarenal, the uppermost of dual renals, or the inferior phrenic, or in a common trunk with the testicular (ovarian, Figs. 2 and 9). Unusual patterns are those in which an inferior phrenic, stemming from the aorta, supplies nearly all the superior, middle and inferior portions of the suprarenals, and in addition, an aortic polar, a capsular branch to the kidney and the testicular (Fig. 9).

*Renal Arteries.*—Typically, and, in most instances (72 per cent of approximately 11,000 kidneys), the kidney is supplied by one renal artery, which arises from the lateral aspect of the aorta and gives off no other branches than those entering the hilum or its borders (Fig. 3). Atypically, parenchymatous branches may arise from the single renal trunk, from its anterior or posterior division or from one of its terminal rami (Fig. 6). Leaving the renal, these branches become distributed variously to the upper or lower pole of the kidney (renal polars), to the anterior or posterior lip of the hilum (perihilar), to any other surface of the kidney or to its fatty capsule. Constant branches of the single renal are the inferior suprarenals (1 to 3). An inconstant, yet frequent branch, is the testicular or ovarian artery, which is a component of the renal pedicle in many

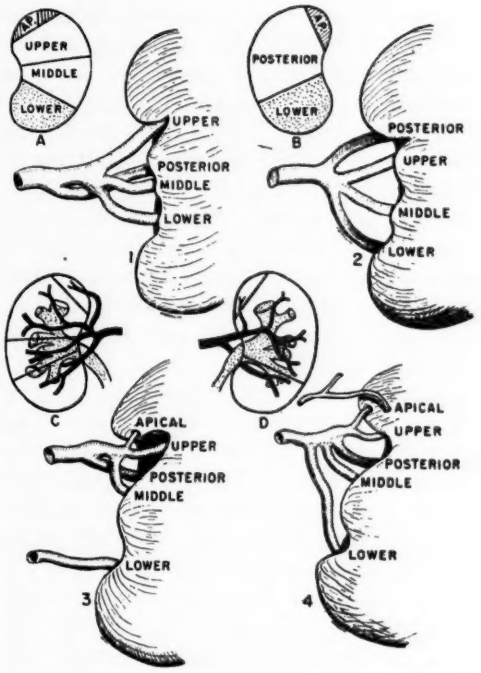



Fig. 14.—Correlation of terminal renal branches with segments of kidney. Sketches *A*, *B*, *C*, and *D* are modified after Graves (1954, 56). *1*, *2*, *3*, *4*, dissection sketches. *A*, anterior view of left kidney; *B*, posterior view. Kidney segments comprise: apical, upper, middle, lower and posterior, only the apical and lower being represented on both anterior and posterior planes. *C* and *D* show intrarenal segmental distribution of renal branches, each segment having its own artery with no collaterals. Dissection sketches: 1. Typical pattern showing 4 segmental branches; the fifth (apical) arises inside kidney, most likely from upper segment. 2. Four segmental branches arising from same point, apical again being intrarenal in origin. 3. Four segmental branches from main renal, apical, a branch of upper segmental, as most commonly the case (Graves). Second hilar branch from aorta becomes lower segmental, as usually so with double hilar arteries. 4. Late origin of posterior segmental branch and a separate origin from aorta of the apical branch.

cases (16 per cent, according to Anson and others, 22 per cent according to Notkovich; see Figs. 7 and 10). Another inconstant, yet frequent branch, is the inferior phrenic, especially from the right renal (Table 1) or from an aortic superior polar (Fig. 9). Surgically considered, an inferior phrenic from the right renal should be carefully inspected and saved, for in some instances it furnishes the entire blood supply to the suprarenal gland (Pick and Anson), or most of it (Fig. 9).

Most commonly, the vertebral level of origin of the renals is at the lower third of the first lumbar level, at the disk between the first and second lumbar and at the cranial third of the second lumbar (Heidsieck). The right and left renal may have the same height level (32 per cent); that of the right is commonly higher (47 per cent), that of the left less commonly so (21 per cent, 100 bodies, according to Taniguchi). In our specimens the renals were at the same level in 30 per cent; the right was higher in 47 per cent, and the left was higher in 23 per cent. A single renal may be present on the right, with multiple renals (2, 3 or 4) on the left, and vice versa, there being no sex or racial difference in this respect (Figs. 5 and 8).

The right renal is longer than the left and nearly always courses behind the IVC. When multiple renals are present, the caudal ones often take a precaval course (Fig. 5). The length of the right renal from aortic origin to its division point varies from 0.5 to 8 cm., that of the left, varies from 0.5 to 6 cm. (Levi). The caliber of the right and left renal is usually the same, the average diameter being 5.5 mm., with variations from 4 to 7 mm. (Hou-Jensen). The diameter of an accessory, i.e., supernumerary, renal artery varies from 1 to 6 mm. and is dependent on the extent of the kidney area supplied, the superior and inferior renal polars often being half the size of the main renal. In instances, the superior and inferior polars have the same caliber as a hilar branch (Fig. 10).

Like the splenic artery, the renal artery may break up into its terminal branches early, i.e., shortly after its origin from the aorta, or late, i.e., near and in the kidney hilum, thus allowing a classification of renal arteries into two main types, viz., the *distributed* with a short stem, and the *magistral* with a long stem, these varieties being comparable to similar divisions of the splenic (Michels, 1942). Division of the right and left renal need not be symmetric, for frequently the pattern is of the distributed type on the right side and of the magistral on the left, and vice versa (Figs. 3 and 5).

In most subjects the single renal artery divides into an anterior and a posterior trunk. Usually this division occurs late, i.e., at about an equal distance between the aorta and the hilum, or in the neighborhood of the hilum. Division of the renal into its two trunks may be precocious, occurring immediately after its origin from the aorta and thereby giving the impression of the presence of dual renals (Fig. 5). The number of subsidiary or principal branches of the renal trunk varies from 2 to 5. Most commonly there are 4 main branches that enter the parenchyma (Fig. 12). Three of these, derived from the anterior trunk, course ventral to the pelvis and were called by Levi (1909) the anterior superior, the anterior medial and the anterior inferior ramus. The fourth main branch, a continuation of the posterior trunk, courses posterior to the pelvis and was, accordingly, called by Levi and Gérard the retropyelic ramus. As a sequence to the discovery of Graves (1954), by means of plastic casts, that the kidney is a *seg-*

*mental organ* composed of 5 segments (apical, upper, middle, lower, posterior), the 3 terminal branches of the anterior division of the renal artery *are now known as the upper, middle and lower segmental branch, since they supply these segments respectively.* The posterior division, a continuation of the renal, supplies the posterior segment. The artery to the apical segment has a varied origin, being derived most commonly from the anterior division of the renal. A fuller discussion of the correlation between the 5 renal segments and the specific arteries supplying them will be given later.

*Supernumerary Renals*: Supernumerary renals occur in about 30 per cent of kidneys, this being the average incidence recorded in the literature on approximately 11,000 kidneys. They may be double, triple or quadruple, either unilaterally or bilaterally (Figs. 6 and 10). Only a few cases in which there were 5 or 6 renals have been reported. Supernumerary renals occur with equal frequency on the right and the left side, there being no significant sex or racial difference in this respect. Variants in the renal arteries of the two kidneys in the same body occur in about 16 per cent of subjects (Kolster, Hellström). Of sides examined, supernumerary arteries occur in 32 per cent, while supernumerary veins are observed in only 14 per cent (Anson and others).

The shortest and most easily understood concept of multiple renal arteries may be expressed in the statement that 2, 3 or 4 right renals may be associated with 2, 3 or 4 left renals, and vice versa. When segmentally arranged, they tend to have the same caliber (Fig. 10). When dispersed to the upper or lower extremity of the kidney, they usually have a smaller caliber than do the aortic hilar renals (Figs. 5 and 6). Multiple renals may be given off by the aorta from the level of

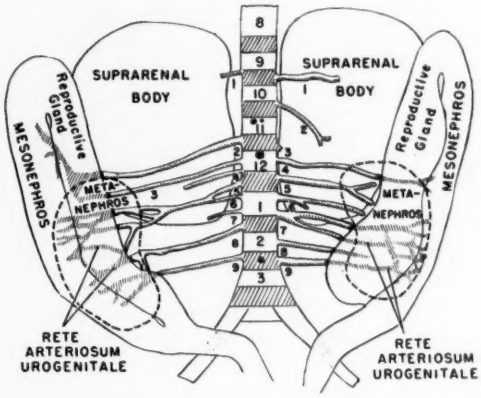



Fig. 15.—Reconstruction of the mesonephric arteries of a human embryo (18 mm). Mesonephroi (Wolffian bodies), reproductive organs and suprarenals are shown. Circles on aorta indicate origin of celiac, superior and inferior mesenteric, the celiac here still being paired. Mesonephric arteries are numbered. The right fifth, sixth, eighth and ninth and the left seventh, eighth and ninth arteries form a coarse-meshed network... the rete arteriosum urogenitale... situated in angle between reproductive organs ventrally, metanephros dorsally and mesonephros laterally. Rete supplies branches to the respective organs and explains the variability in point of origin from aorta of the persisting arteries that arise from the roots of this network. (Modified after F. Hix in Manual of Human Embryology, Keibel and Mall, Lippincott, 1912, vol. 2, p. 822, fig. 572.)

the superior mesenteric to that of the inferior mesenteric or as high as the aortic diaphragm, and as far inferior as the hypogastric artery (Fig. 11). The distance between the aortic site of origin of the supernumerary renals varies considerably, the shortest being 0.7 cm., the longest 8.9 cm. and the average 2.79 cm. (Anson et al).

As a guide to translumbar arteriographic study and to insure *complete filling of all renal arteries with a contrast medium,* it is important to know that the vertebral level of origin of supernumerary renals may vary from the eleventh thoracic to the fourth lumbar. When triple or quadruple, they may be segment-

ally arranged along the second, third and fourth lumbar levels. In their course to the kidney; the upper supernumerary renals may be retrocaval and the lower ones precaval (Fig. 10). Usually, as they course transversely, they are parallel and enter the hilum and kidney in the sequence of their origin, but in some instances the upper hilar renal crosses the lower one to reach the hilum (Fig. 7).

Dual renals from the aorta to the hilum occur rather frequently (10 per cent of 11,000 kidneys; Figs. 5 and 6). They may arise contiguously, side by side or one in front of the other, or they may be spaced far apart, in the latter instance entering the extreme ends of the hilum (Fig. 8). Dual renals are frequently represented by a pattern, in which, in addition to the main aortic hilar renal, there is a superior or inferior aortic or renal polar (Figs. 4 and 5). Very rarely, the lower of dual renals arises from the bifurcation point of the aorta or from the common iliac. In cases of dual renals, both may pass in front of the pelvis or the upper may pass behind and the lower in front of the pelvis, or partly in front and partly behind thereof. The upper renal may cross the lower one, then cross the ureteropelvic juncture to reach the inferior pole of the kidney (Fig. 7).

Triple hilar renals derived from the aorta are, relatively considered, infrequent (1 to 2 per cent). The pattern of triple renals in which 2 are hilar and of aortic origin and the third is either a superior or lower polar occurs rather frequently (Fig 10). The superior or intermediate of the triple renals may supply a superior polar or a suprarenal branch; the inferior may give off the testicular (ovarian) or an inferior polar. Quadruple hilar aortic renals do occur, but reports thereof have been few. In the usual quadruple pattern, the four renals arise from the aorta in segmental sequence, their point of origin being from that of the superior mesenteric to that of the inferior mesenteric (Anson). The upper two renals may have a postcaval course, the lower two a precaval one. The upper two may pass in front of the pelvis, the lower 2 behind it. Four renals to the kidney can be effected by a variety of combinations, as 2 hilar and 2 polar, 3 hilar and 1 polar, 3 polar and 1 hilar (Figs. 10 and 11). The four renals occasionally have the same caliber, but more frequently only one of them is large, the others being smaller and distributed to the upper and lower extremity of the kidney.

*Superior Polar Arteries*: These are usually single and arise separately from the aorta (7 per cent) or as a branch from the proximal, middle or distal portion of the renal (12 per cent; see Figures 2, 5 and 6). They may be double or triple, unilaterally, or bilaterally, with a varied aortic or renal source of origin for each (Fig. 6). Often, they arise from an inferior suprarenal or from its adipose capsular branch to the kidney (Fig. 4). In instances, they arise from the inferior phrenic or from the superior mesenteric (Fig. 9). Frequently, they give off several branches to the suprarenal gland, a fact to be remembered in the removal of the latter (Figs. 2, 4 and 6). Before entering the parenchyma, they often break up into a leash of branches that enter the superior pole like piercing needles.

Surgically considered, superior polar arteries present many hazards. They are often high and cryptically concealed, and, accordingly, may be mistaken by touch for strands of connective tissue of an ordinary renal pedicle. When inadvertently torn, they produce massive hemorrhage, at times immediately fatal (Eisendrath). When they are ligated, anemic infarcts are produced in the devascularized area

with resultant necrosis, for renal arteries are, like the hepatic and splenic, end arteries in the strictest sense (Morison, 1925).

*Inferior Polar Arteries*: These are predominantly single and are derived either from the aorta (5.5 per cent, or as branches of the renal artery (1.4 per cent). (See Figs. 10 and 11.) Occasionally they take origin from the suprarenal, common iliac and superior mesenteric arteries. They may have a high origin from the aorta, then cross lower renal arteries to reach the inferior extremity of the kidney. In some instances they are double, one arising from the aorta and the other from the renal artery, or the two from either source. They may or may not be accompanied by a vein (Fig. 10). As was ascertained by Graves (1956) in plastic casts of the kidney, the inferior polar artery supplies the lower segment of this organ, while the superior polar vascularizes the apical segment, both arteries *being end arteries*, i.e., having no collateral circulation from the other segments of the kidney.

Clinically and surgically considered, the inferior polar arteries are extremely important, being in many instances, a fundamental anatomic factor in the causation of hydronephrosis. That an anomalous blood vessel, such as the inferior polar artery, may cause renopelvic distention by constricting (through kinking) the upper part of the ureter or the ureteropelvic juncture, with intermittent abdominal pain, as a sequence to retention of urine, is definitely known; the clinical entity has been verified anatomically and corrected surgically by severance of the obstructing vessel in thousands of cases (Mayo, 1903; Ekehorn, 1907; Capolare, 1929; Eisendrath, 1930; Walters, 1933; Hellström, 1934; Winsbury-White, 1936; Jewett, 1939; Dege, 1939; Edsman, 1954, and many others).

*Correlation of the Renal Arteries to the Segmental Division of the Kidney.*— In an investigation of 70 plastic corrosion casts made of autopsy kidneys, and on the basis of 60 renal arteriograms thereof, Graves of King's College, London (1954-1956), for the first time gave evidence that the kidney, like the lung and liver, is a segmental organ. The parenchyma of every kidney is divisible into 5 segments, these being the apical, the upper, the middle, the lower and the posterior. The apical segment occupies the medial side of the upper pole, mainly on its anterior surface, a bit of it being in the posterior plane. The upper and middle segment lie in the anterior plane. The lower segment, constituting the lower pole of the kidney, lies both in an anterior and posterior plane. The posterior segment lies entirely in a posterior plane and occupies an area between the posterior part of the apical segment and the posterior part of the lower segment.

Each of the 5 segments of the kidney has its own specific blood supply furnished by a separate vessel variously derived from the renal artery, the aorta or elsewhere. Typically, the anterior division of the renal gives rise to the upper, middle and lower segmental arteries, the apical segmental artery, in most cases, likewise, arising from it. The posterior division of the renal artery supplies only the posterior segment, but in some instances (10 per cent), gives off the apical artery. The posterior segmental artery, a continuation of the posterior division of the renal, after crossing the upper border of the pelvis, courses behind and in close association with the juncture of the upper calyx and the pelvis . . . *a landmark which is constant.* Running under the lip of the hilum, the artery forms a curve from which branches are given off laterally. These comprise three groups: upper (1 or 2), middle and terminal. Inside

the kidney the lower segmental artery divides into an anterior and a posterior branch. The middle segmental has terminals that interdigitate with those of the posterior division. The upper segmental artery arises either in the hilum or under the hilar lip and divides intrarenally into two branches.

The apical segmental artery (superior polar) has the most varied sites of origin. In order of frequency, it arises from the trunk of the anterior division or the upper segmental artery (43.3 per cent), from the junction of the anterior and posterior division of the renal (23.3 per cent), from the renal stem or aorta (23.3 per cent) and from the posterior division (10 per cent). In about one-third of the specimens an accessory renal, most frequently derived from the posterior division, enters the posterior aspect of the apical segment.

Variations in the origin of the other segmental arteries may be classified into three groups: (1) lower artery arises first from the renal, anywhere from the aorta to the hilum, or separately from the aorta, while the upper and middle segmental artery have a common origin (53.3 per cent); (2) lower artery arises with the upper, the middle coming from the lower (16.6 per cent); (3) upper middle and lower segmental arteries arise from the same point (16.6 per cent).

Thus, in view of Graves' pioneer discovery of the segmental structure of the human kidney and after centuries of effort on the part of hundreds of investigators, the variational anatomy of the renal arteries is finally understood and solved. Inside the kidney there is a *constant arterial pattern, for each of the 5 segments of the organ has its own specific blood supply, with no collateral branches to neighboring segments.* The baffling variational anatomy of the arteries in the renal pedicle, the varieties of terminal branching at or near the hilum, the presence of supernumerary renals (2 to 4) in the renal pedicle, and the occurrence of superior and inferior polar arteries stemming from the renal artery or the aorta are phases of renal vascularization, that now are definitely understood and solved. Graves emphasized the fact that the intrarenal distribution of the renal arteries are arteriographically identifiable, as *there is always a constant pattern present,* irrespective of the variational anatomy of the origin of the segmental arteries. The next point emphasized is that the 5 segmental arteries to the kidney *are readily accessible to the surgeon at operation, for they may actually be seen at the hilum* and by temporary compression of the renal vessel, which produces a purplish discoloration of the area supplied, one can readily determine which specific segment of the kidney the compressed artery supplies. Multiple (supernumerary) renals no longer offer any difficulty, for, while their distribution *is constant* in the kidney, it is only a matter of understanding the underlying embryologic aspects of the vascularization of the kidney, that sense, order and understanding can be made of the varied blood supply to the kidney (Fig. 15).

The final and most beneficial results of Graves' discovery of the segmentation of the kidney are, after all, of extreme surgical importance, for, with knowledge of the segmentation of the kidney, resections of areas of tuberculosis and of calculi can now be performed on *a segmental basis without loss of the entire kidney.* Next in order of importance is the proper and sole way to open the kidney (nephrotomy). Hyrtl (1882) was the first to show that there was a natural division line (natürliche Teilbarkeit) between the two arterial trees, made respectively by the anterior and posterior primary divisions of the renal artery. Brö-

del (1901) substantiated this contention with corrosion casts, maintaining that the anterior division of the renal supplies three-fourths of the kidney, while the posterior division supplies only one-fourth. To avoid severance of the collecting tubules of the posterior pyramids and to attain an avascular area, Brödel suggested that the incision in a kidney should be made along the kidney's lateral convex border, a bit posterior to its midline. Now, on the basis of a thorough knowledge of the intrarenal segmental distribution of the renal arteries, Graves has concluded that the area involved in this incision method of Brödel is *by no means a bloodless area.* Graves suggested that if an incision is made on a radial and intersegmental plane, it may prove to be less vascular at operation.

Opposed to Graves' roentgenographically undeniable demonstration of the specific and constant segmental pattern of the adult kidney, and apparently without knowledge of his pioneer discovery, Smithuis (1956), on the basis of a study of 100 plastoid corrosion specimens, maintained that, although there is a natural divisibility between the ventral and dorsal lobes with their respective arteries (Hyrtl, Brödel), the unit structure of the kidney itself (the lobe), precludes any uniform segmentation of the organ, for the renal lobe comprises a pyramid with the cortical layer above it. While it is desirable to accept the renal lobe as the basis of possible renal segmentation, a study of the internal vascularization shows that no renal lobe has an independent arterial blood supply, since every lobe is supplied with blood from at least two sides, this via interlobar arteries and arciform rami. Smithuis admitted that in the adult kidney there are, in many cases, remnants of neonatal surface renal markings (grooves and white lines) localizing the division between the superior pole and the central part of the kidney and between the latter and the inferior pole, but the surface projection lines, in his opinion, are surgically meaningless, from the point of view of the embryonic structure of the kidney, the renal lobe has always been identified as the basis of renal segmentation.

And thus, with small differences of opinion as to the exact character of the segmental division of the adult kidney, the conclusion has finally been arrived at and is fully warranted, even on the basis of a first attempted statistical analysis of extrarenal dissections correlated with renal segmentation (Fig. 14), that aberrant renal arteries are normal renal vessels that have a precocious origin either from the renal artery, the aorta, or some other source, and that severance of any renal artery will produce necrosis of the area it supplies. Like accessory hepatic arteries and ducts (Michels, 1955), accessory renal arteries are not accessory but are life-sustaining vessels, aberrantly derived and aberrantly entering the kidney.

*Horseshoe Kidney.*—This type of kidney was first described by Bérenger de Carpi in 1522, as the "ren unguliformis." Later many authors used the term "renes arcuati." Data on the incidence of the horseshoe kidney vary considerably. Botez (1912) tabulated the observations of 184 authors to a total of 51,504 autopsies and noted an incidence of 1:715. Legueu and Papin (1912) reported a ratio of 1 to 500 or 600. Lipshutz and Hoffman (1918) of this Institute, in an analysis of 70,502 cases of fused kidneys reported in the literature, noted that 105 were horseshoe kidneys (1:671). Bell (1950), in an evaluation of 59,064 postmortems at Minnesota University, found 119 cases (1:497). Fetter, Varano and Ayres (1956), in an analysis of 4,093 autopsies at the Jefferson Medical College, found 12 cases (1:345), with a sex incidence of 84 per cent for male and 17 per cent female. In

urographic examination of 13,080 subjects, Lowsley (1952) observed the anomaly in pyelograms in 46 cases (1.284), while Dees (1941) observed 4 instances pyelographically in 1,410 patients (1:352). Gutierrez (1934), estimated a ratio of 1 in 100 or 200 pyelograms. A variation of the horseshoe kidney is the dumbbell or disk-shaped kidney with fusion in the middle, the fusion, like that of the horseshoe type, having occurred (Fig. 14) before the kidney grew out of the pelvis (Pohlman, 1905).

Both types of fused kidneys always have strikingly aberrant renal arteries, the number of which varies from 2 to 6. Characteristically, they are excessively long or short. They may be derived variously from the aorta, the testicular (ovarian) artery, the common iliac, the middle sacral, the external or internal iliac, and the superior and inferior mesenteric arteries and the bifurcation point of the aorta, the isthmus, in many instances, having a separate blood supply via one or two vessels (Fig. 13). According to Papin (1928), there are reports in the literature of some horseshoe kidneys having 7 (3 cases), 8 (2 cases) and even 10 (2 cases) renal arteries. A description and seven illustrations of the blood vessels in fused kidneys was published by Robinson in 1909. On the basis of 60 specimens, it was noted that in 20 per cent the isthmus had a distinct blood supply, it being effected by a single vessel in 13 per cent. Herman and Fetterolf (1913) described and illustrated the vascularization pattern of a dumbbell kidney that had 7 arteries, 4 of which came from the aorta, 1 from each common iliac and 1 from the left testicular artery (Fig. 14).

Fetter, Varano and Ayres (1956), in their exhibit on horseshoe kidney, indicated the various methods now being employed to detect this anomaly by roentgen diagnostic studies, scout films, intravenous urographic and retrograde pyelographic studies, retroperitoneal pneumographic and pyelographic studies and the pyelographic angle of Gutierrez (1942).

*Blood Supply of the Pelvis, Calyces and Ureter.*— Anatomic knowledge of the diverse vascularization patterns of the cited structures is meager yet clinically and surgically important. Among the most recent contributions are those of Michaels (1948), Daniel and Shackman (1950), and Douville and Hollinshead (1955). According to the last-mentioned authors, the vascular network of the renal pelvis is markedly different from that of the ureter, being formed by anastomosing branches of several stem arteries derived from the renal artery at different levels. Communications between the arteries are so numerous that dangerous interference with the blood supply to the pelvis, surgically considered, seems unlikely.

As to the blood supply of the ureter, Fitel (1895) was among the first to state that the arteries to the upper part of the ureter comprise derivatives from the renal artery, the aorta, and the common iliac and hypogastric arteries and reaches the ureter on its medial side, whereas the arteries supplying the distal part of the ureter are derived from the testicular, vesical, uterine and vaginal branches and reach the ureter on its lateral side.

By means of injected specimens, Michaels showed that the ureter receives its main blood supply through long arteries that arise from the lower end of the aorta and the common iliac and hypogastric arteries. The lower end of the ureter, close to the bladder, commonly is supplied by an artery derived from the vesicodeferential branch of the hypogastric or from the inferior vesical. Reaching the ureter, the long arteries divide into ascending and descending branches that anastomose with similar branches derived from the renal, testicular or ovarian arteries, while

below they communicate with branches from the uterine, vaginal, superior and inferior vesical and, occasionally, middle hemorrhoidal arteries. From the pelvis to the bladder the long arteries give off secondary branches that ramify around the ureter and anastomose with one another and with upper and lower branches. Tertiary branches, given off by the secondary branches, pierce the musculature of the ureter. In some instances, the long ureteral arteries are double or even triple.

Daniel and Shackman (1952), in an investigation of 50 ureters by means of an injection medium, noted that the blood supply of the right and the left ureter is seldom symmetric and that there is a marked variation in individual persons. Typically, the ureter is supplied by long arteries derived from the aorta or its branches. Traveling in the loose adventitial tissue of the ureter close to the peritoneum, they divide into ascending and descending branches, which anastomose. From the plexus thus formed, small twigs are given off to the ureter. Sources of origin of the long ureteric arteries comprised: renal artery, 98 per cent; upper and middle segment of the aorta, 18 per cent; ovarian artery, 8 per cent; testicular artery, 30 per cent; lower part of aorta, 26 per cent; common iliac artery, 25 per cent; internal iliac artery, 15 per cent, and uterine, inferior and superior vesical arteries, 98 per cent. Authors maintain that the ureters may be divided at any point if they have large arteries with large anastomoses, but when the anastomotic branches are minute they can be divided only at or above the vascular anastomosis. When the intermediate part of the ureter is supplied by minute peritoneal twigs, its separation from the overlying peritoneum for more than 2.5 cm. may produce ureteric ischemic necrosis. The latter process will eventuate in 10 to 15 per cent of subjects in any method of ureterocolic anastomosis in which the ureter is always *standardly divided at the same point* or mobilized for more than 2.5 cm. Daniel and Shackman concluded that the ureter may be safely divided 2 cm. below the point of entry of a pulsating long ureteral artery. In the absence of the latter it can be effected 2 cm. below bifurcation point of the common iliac. In ureterocolic anastomosis, deprivation of the blood supply to the ureter in and about the point of anastomosis produces sloughing and, if the anastomosis is intraperitoneal, peritonitis and death. Excellent illustrations of the blood supply of the ureter are presented in the atlas of Grant and that of Anson as well as in Philip Thorek's text *Anatomy in Surgery.*

*The Gonadal Arteries (Testicular or Ovarian).*—Variations in the origin and course of the gonadal arteries have been described by many authors (Kolster, 1902; Gérard, 1913; Adachi, 1928; Cordier and his associates, 1938; Anson and others, 1940-1955; Martin, 1955, and Notkovich, 1956). The last-named author published the largest and most extensively illustrated treatise thereon.

Testicular or ovarian arteries (which have no sexual difference of origin), prevailingly arise from the anterior surface of the aorta below the renal vein; less commonly, behind or above the latter (Figs. 4 and 10). In about 15 per cent they arise from the renal artery, from one of its branches or from a supernumerary renal (Figs. 6 and 13). The right gonadal may stem from a renal, the left from the aorta or vice versa (Fig. 6). Occasionally a gonadal artery may arise from a suprarenal, phrenic, superior mesenteric, lumbar, common iliac or hypogastric artery. Aberrantly, a testicular artery may supply an inferior suprarenal branch (Figs. 7 and 10). In many instances (17 per cent), the gonadal arteries are double on one side; less frequently,

on both sides. In such cases both arteries may have either an aortic or renal origin, or the two may be derived from the same source. As a rule, the inferior of dual gonadals is of aortic origin, the superior being either from the aorta or the renal artery. Occasionally, gonadal arteries arise from the aorta by two or three roots. Their vertebral level of origin varies from the first to third lumbar level (Adachi).

*Arched Gonadal Artery:* Of surgical and clinical import is the fact that gonadal arteries, by crossing the renal vein (Fig. 10) are frequently components of the renal pedicle (18 per cent, Pick and Anson; left side, 34 per cent, right, 16 per cent; Notkovich). In an investigation of 183 dissections, partly made in the Anatomical Laboratories of the Jefferson Medical College, Notkovitch (1956) classified the gonadal arteries into three types, according to their relation to the renal vein. Testicular or ovarian arteries may arise from the aorta or the renal artery: (a) behind or below the renal vein; (b) above the level of the renal vein, or (c) behind or below the renal vein, but, instead of descending, the artery on the left ascends behind the renal vein, curves over its upper border (lateral to the suprarenal vein) and then descends in front of it (Fig. 10). The latter type (22 per cent) constitutes the well-known *arched testicular (ovarian) artery* of Luschka (1864), so important in urology. The looped course of the gonadal artery may be in front of the renal vein when the latter passes behind the aorta.

Anson and Kurth (1955) likewise stressed the fact that the testicular artery presents more unfamiliar relations on the left than on the right. According to their observations, the artery may accompany the renal in the middle half of the renal pedicle, hook around the renal vein, pass through the latter in a hiatus (3 per cent), or over a tributary thereof, loop around a lumbar tributary and course through the arms of a bifid testicular vein.

Clinically considered, it is to be noted that the arched gonadal artery may be a pathologic factor in compression of the renal vein, or be a possible etiological factor in idiopathic varicocele in the male and ovarian varicocele or varicocele of the broad ligament in the female. The arched gonadal artery may likewise be a factor in orthostatic albuminuria and, by compression of the renal vein, have a direct influence on the direction of the blood flow from the kidney and gonads (Fagarasanu, 1938); (Notkovich, 1956).

As important additive information to the present contribution, it should be noted that Anson and his co-workers (1940, 1947, 1948), have shown that the renal vascular elements are not isolated from the blood vessels of the neighboring organs and regions, and that the achitectural patterns of renal arteries differ strikingly from those of the renal veins, this being especially the case with the left renal vein. Upon it converge tributaries not only from neighboring viscera, *but on a retroaortic, prevertebral level, via lumbar veins (segmental and ascending, hemiazygos) from parital structures as well,* thus bringing blood to the left kidney from the musculature of the dorsal abdominal wall, vertebral column, spinal cord, thorax, *pleura, pericardium* and *pelvis.* Collateral routes are thereby opened for spread of infections to different regions of the body as illustrated with 33 figures in the unmatched classic monograph of Fagarasanu of France (1938). The functional role which the *vertebral veins* play in the spread of metastasis, was clearly outlined by Batson (1940).

*Embryologic Aspects.*—A short resumé of the embryologic background of the kidney and suprarenal gland as studied by Broman (1908, 1927) and Felix (1912) will help clarify the reasons for the varied

blood supply of the respective organs. When the suprarenals are first formed in the urogenital ridge, they are in immediate vicinity of the cranial end of the primitive renal and gonadal organs (ovary, testis). While the main branches (two or three) of the primitive kidney (pronephros) undergo atrophy with its retrogression, the collaterals of these to the suprarenal glands increase in size and so become transformed into the suprarenal arteries. These primitive relations are soon lost, for the pronephros is replaced by the mesonephros, which as a large mass (urogenital ridge) extends caudally from the eighth cervical to the twelfth thoracic segment, receiving, through these levels about twenty mesonephric arteries from the lateral side of the aorta (Fig. 15). Branches of three mesonephric vessels, near the first and second lumbar segment, become the three suprarenal arteries. With the retrogression of the mesonephros (Wolffian body) they persist as independent branches of the aorta. The lower of these eventually takes over the blood supply of the permanent kidney and becomes the renal artery. The upper takes over the blood supply of the diaphragm and becomes the inferior phrenic. As a result of differential growth, the definitive suprarenal arteries become branches of the renal and inferior phrenic, thus reversing the original embryonic conditions. Since the inferior phrenic, suprarenal and gonadal arteries are derivatives of the original mesonephric vessels, varied types of origin of the listed arteries may be expected, e.g., origin of gonadals from the renal or suprarenal, origin of suprarenals from the aorta or renal, common trunk for the renal and inferior suprarenal, common trunk for the inferior suprarenal and superior polar, inferior suprarenals from the superior polar and the reverse thereof, etc. The varied sites of origin of the gonadal arteries from the aorta (below, above or under the renal vein) can readily be explained by the fact that gonadal arteries are persistent branches of the mesonephric arteries that develop cranial or caudal to the renal pedicle. By crossing the latter with the descent of the testis, the arched gonadal artery (one that loops over the renal vein) is formed, as is normally the case in fishes, in which the elongated kidney is the mesonephros and receives numerous branches from the aorta (Gray, 1906).

The seemingly baffling variational anatomy of the renal blood supply by supernumerary vessels may readily be understood when one recalls the investigative work of Felix (1912). He noted that in the upper lumbar region the mesonephric arteries form a network, the rete arteriosum urogenitale, from which the gonads, the mesonephros and the definitive kidney (metanephros) are supplied by segmentally arranged arteries (Fig. 15). Aberrant renal arteries, arising separately from the aorta, may be regarded as persistent mesonephric arteries, whereas renal arteries having a proximal origin in the renal pedicle or at the hilum may be regarded as variations or degeneration of the primitive segmentally arranged mesonephric arteries. At about the second month the kidney anlage rotates on its longitudinal axis, so that its former ventral-facing hilum becomes directed medially, as in the adult. Atypically, through overgrowth laterally or medially, the renal hilus may assume a dorsal position (Priman, 1929). In an ectopic kidney or a horseshoe kidney that has failed to ascend out of the pelvis the hilum still faces forward and the blood supply is derived from regional arteries, such as the distal end of the aorta or the middle sacral, common iliac or hypogastric artery.

In conclusion, it should be stated that aberrant vascularization of the kidney may be due to developmental peculiarities,

malformation, rotation, migration or fusion of the kidney. Varieties comprise: (1) ectopic kidney in the iliac fossa, at the brim of the pelvis, in the pelvis or crossed renal ectopia, the kidney then receiving, in many cases, its blood supply from the common iliac or its branches; (2) unilateral kidney with no renal vessels on the agenetic side, although some portion of the ureter may be present; (3) unilateral dwarfed kidney or bilateral hypoplasia with modified renal arteries; (4) unilateral or bilateral polycystic (large) kidney with varied blood supply; (5) unilateral fused kidney (elongated) with marked variations in the course of the renal vessels and sites of their origin; (6) anomalies in form and position of the renal pelvis and calyces, often accompanied by anomalous distribution and origin of renal vessels, and (7) unilateral or bilateral, complete or incomplete duplication of the pelvis and ureter, these being common phenomena attended with marked variations in the renal blood supply. Further data on developmental anomalies of the kidney are to be found in the pioneer and classic investigative work of Polhman (1904, 1905).

The current concept of the varied and amazingly copious blood supply of the suprarenal glands and its intimate relation with the renal blood supply should, in addition to its surgical import, open new avenues of physiologic and cardiovascular research. Among the anatomicoclinopathologic integrations may be listed: (1) nephroptosis or torsion of the kidney associated with an aberrant renal vessel (usually an inferior polar artery, occasionally a vein); (2) hydronephrosis, due to occlusion or compression of the ureter or the ureteropelvic juncture by an inferior polar artery; (3) varicocele secondary to compression of the renal vein by an arched gonadal artery, usually on the left side, and (4) hemodynamic disturbances of the renal arteries and arterioles in cases of hypertension, for it has repeatedly been shown that renal ischemia plays an important role in arterial hypertension. Constriction of the renal arteries, presumably, causes release of a pressor substance (hypertensin, angiotonin or renin of the old school) to the general circulation. The substance can be withheld from the circulation by closure of the renal vein.

Interesting in this connection are the investigations of Trueta and his associates (1947). In experiments with rabbits, they showed that in the crush syndrome the original injury may cause spasm of the main arteries of the affected limb and that this spasm may extend proximally and involve the renal artery and its branches. Constriction of the latter at the corticomedullary juncture shunts the blood from the outer cortex through the inner cortex and medulla, thereby producing cortical ischemia. Correctly interpreted, according to Trueta, the blood diverted from the outer cortex flows through an alternative renal medullary bypass mechanism composed sequentially of: afferent arterioles of the juxtamedullary glomeruli, the capillary tufts of these glomeruli, their efferent arterioles, the vasa recta derived from them and, finally, the interlobular veins. The existence of such a medullary bypass mechanism or shunt was ascertained by More and Duff (1944) by means of neoprene casts of human autopsy kidneys. The problem of arteriovenous shunts in the kidney is largely unsolved. While these may be present in a random and insignificant manner, Trueta noted that they are extremely uncommon, whereas More and Duff found no evidence for them at all as claimed by Spanner (1937) and others.

Also unknown is the extent of collateral circulation to the kidney. Attempts at induction of a collateral circulation to the kidney (e.g., nephro-omentopexy, denerva-

tion procedures), have definitely been abandoned for hypertension (Fishberg, 1947). In experimental animals, revascularization of the kidney has been essayed not only with omentorenopexy (McNider and Donelly, 1939), but with myorenopexy (Bruger and Carter, 1941), enterorenopexy (Katz, Hannon, Alden and Baronfsky, 1954) and splenorenopexy (Weeks, Steiner and Victor, 1946). Most recently, Davis and Moore (1957) made a direct implantation of the splenic artery into the cortex of the left kidney in 5 dogs. After two months, examination with both methylene blue and iodopyrant, injected through the splenic artery and filling the renal arterial tree, showed that a collateral circulation had been established between the splenic artery and the renal artery. The best collateral circulation was obtained in dogs, in which the kidney had been rendered partly ischemic by ligating a major renal vessel. The mechanism of recanalization and mode of formation of the collateral blood flow, however, were not ascertained.

A possible route of collateral renal circulation is via the adipose capsular branches given off by the renal and suprarenal arteries, for they could readily terminate in the long-forgotten subperitoneal arterial plexus of Sir William Turner (Figs. 2 and 8). In 1863 this anatomist showed that numerous branches given off by the renal and spermatic arteries in the lumbar and iliac regions join the plexus. This view was substantiated by Hughes (1892), who presented an illustration of the capsular branches terminating in the extraperitoneal fat. Albarran (1909) in his classic book on the kidney, offered an illustration of the perirenal arterial circle formed by adipose capsular arteries, which he classified into the following groups: (1) renal; (2) mesenteric; (3) spermatic; (4) capsular; (5) lumbar, from the third level to the posterior capsule; (6) aortic, and (7) inferior phrenic. The anatomic and physiologic character of the perirenal arterial circle deserves extensive investigation, especially in view of the possible significant role of the subperitoneal plexus and the capsular adipose branches of the kidney in renal collateral circulation. Inside the kidney, as was shown by Graves (1954) in 70 plastic casts and in arteriograms, there is no collateral circulation, since each of its 5 segments (apical, upper, middle, lower, posterior) has its independent blood supply furnished by a specific branch from the renal artery, aorta or, aberrantly, from some other source. Inside the kidney, as was clearly demonstrated by Morrison (1926) by means of injected celluloid preparations (depicted in 37 figures), each branch of the renal artery is, in itself, a closed circuit or end artery.

Finally, the problem of acute renal failure due to renal ischemia, so devastatingly fatal (90 per cent) to wounded men during the Korean war (mortality rate subsequently reduced to 50 per cent) has not yet been solved on an anatomicophysiologic basis. The latest contribution thereto, is a plan of treatment with papaverine hydrochloride, as investigated by Johnstone and his associates (1956) via experiments on excised kidneys of rabbit and man that were attached to an artificial heart-lung machine. Reversal of acute renal failure was attained in 10 patients with this drug, but the anatomic rationale of the improved circulation induced in the kidney remains unclear, for it is not yet known whether changes in the renal vessels that reduce blood flow (narrowing and closure of small renal arteries and arterioles) are organic or spastic. According to Bell (1950), certain forms of renal ischemia may be due to a spastic rather than to an organic change in the renal vessels. In over 20 per cent of typical clinical cases he observed no structural changes

in the arterioles, nor was there a greater involvement of the large and small renal arteries thán that noted in nonhypertensive controls. From this, Bell concluded that, in a large percentage of cases of primary hypertension, renal ischemia cannot be explained on an anatomic basis. In other words, renal ischemia is "not the cause of primary hypertension but the effect of a spastic state of the renal arterioles."

SUMMARY

The varied blood supply of the kidney was investigated in a dissection of 185 kidneys, obtained from adult bodies in the dissecting room. The adrenal and inferior phrenic arteries were studied in 50 cadaver specimens, which comprised the entire regional area removed *en bloc* and then dissected in detail. To an extent never attempted before, the authors correlated their observations with those recorded in the world's literature during the past seventy-five years . . . about 150 papers, fully read and cited, comprising the review.

The adrenal blood supply varies to such an extent that it is never the same in any two bodies or in any two sides. It is not effected by 3 single stem arteries, as maintained in textbooks for over one hundred years, but comprises (1) from 4 to 30 superior adrenal vessels of twig size, derived from the inferior phrenic trunk or its posterior division; (2) a middle adrenal vessel, prevailingly from the aorta but frequently lacking or replaced by another artery; (3) an inferior adrenal vessel, predominantly of single renal origin but in many instances multiple and of varied origin (aorta, renal, superior polar, capsular branch of kidney). The adrenal blood supply is intimately related to that of the kidney, for the adipose capsular branch to the kidney frequently gives rise to an inferior suprarenal. The latter in turn, may give off renal polar vessels and capsular branches.

From a statistical study of 11,000 kidneys reported in the literature, and on the basis of 185 dissections made by the authors, the conclusion was drawn that the renal artery is single in 72 per cent and double in 10 per cent of cases. Triple or quadruple renal arteries occur, but rarely. Superior polar arteries arise from the aorta in 7 per cent of cases and from the renal artery in 12 per cent. Aortic inferior polar arteries occur in 5.5 per cent, renal arteries in 1.4 per cent

Graves of London, by means of plastic corrosion casts, has recently shown that the kidney is a segmental organ, like the lung and the liver. The segments of the kidney are the *apical*, the *upper*, the *middle*, the *lower* and the *posterior*. The authors correlated their observations on renal arteries with this concept and confirmed the contention of Graves, to wit, that the arterial pattern inside the kidney is constant, irrespective of the varied origin of the segmental artery. Like so-called accessory hepatic arteries and "accessory" hepatic ducts, accessory (aberrant) renal arteries are *normal structures*. Anatomically and functionally considered, they have a precocious origin from the renal trunk, the aorta or some other source, *and severance of any renal artery produces necrosis in the area it supplies, as is likewise the case when an aberrant hepatic artery is severed.*

An account is given of the blood supply of the horseshoe and the disc-shaped kidney and that of the pelvis, calyces and ureter. The surgical hazard of the arched *gonadal artery*, so frequently present (16 per cent) in the renal pedicle, is emphasized. The multiplicity of renal arteries is explained on an embryologic basis, the encountered varieties being full remnants or partially degenerated primitive mesonephric arteries. On the basis of the world's literature on the renal blood supply, many anatomicoclinocopathologic in-

tegrations are made, such as the medullary by-pass mechanism of Trueta, the possible routes of collateral circulation to the kidney and assayed attempts thereof, renal ischemia and its relation to primary hypertension and acute renal failure. The new roentgen anatomic picture of the renal arteries is discussed, with ample references to the preoperative surgical import of renal arteriograms.

RESUMEN

Los autores han estudiado las variaciones en la vascularización renal disecando 185 riñones de cadáveres de adultos procedentes de la sala de disección. Estudiaron las arterias suprarrenal y frénica inferior en cincuenta piezas de la región extirpada en bloque y disecada al detalle. Los autores, en un intento no llevado a cabo hasta hora, comparan sus observaciones con las registradas en la literatura mundial durante los últimos 75 años y leyeron y citan detalladamente no menos de 150 trabajos.

La vascularización suprarrenal es tan variable que nunca se encuentra on una distribución igual en dos individuos y ni aún en los dos lados en el mismo sujeto. No depende de tres simples trocos arteriales como ha sido sostenido por cientos de años en los libros de texto, sino que comprende: (1) de 4 a 30 vasos suprarenales finísimos derivando del tronco de la frénica inferior o de su rama posterior, (2) de la suprarrenal media, derivada de la aorta pero a veces faltando o naciendo de alguna otra, y por último (3) de la suprarrenal inferior originada predominantemente solo en la renal, pero muchas veces de variado origen (aorta, renal, polar superior o rama capsular del riñón). La circulación sanguínea suprarrenal está intimamente en conexión con la del riñón por intermedio de la rama de la cápsula adiposa que frecuentemente da origen a la suprarrenal inferior. De esta última, a su vez, pueden proceder los vasos polares y los ramos capsulares.

A partir de un estudio estadístico de 11.000 riñones registrados en la literatura, y sobre la base de 185 disecciones practicadas por los autores, se deduce la conclusión de que la arteria renal es única en un 72% de los casos y doble en un 10%. También se presentan arterias renales triples o cuádruples, pero raramente. La arteria polar superior sale de la aorta en el 7% de los casos y de la renal en el 12%. Un 5% de veces la polar inferior es de origen aórtico.

Graves, de Londres, por medio de moldes plásticos de corrosión ha demostrado recientemente una distribución segmentaria en el riñón afín a la del hígado o del pulmón. Los segmentos del riñón serían: apical, superior, medio, bajo y posterior. Los autores cotejando, sus observaciones con este concepto, y confirmando las ideas de Graves, llegan a la conclusión de que la distribución de la circulación intrarrenal es c o n s t a n t e independientemente del origen variable de las arterias segmentarias. De la misma manera que existen arterias hepáticas accesorias y conductos hepáticos "eccesorios" las arterias renales accesorias (aberrantes) son estructuras normales. Estas arterias tienen, anatomica y funcionalmente consideradas, un origen precoz en el tranco renal: la aorta o algún otro punto de partida y si se seccionan dan origen a necrosis del area de distribución correspondiente, cosa que ocurre de la misma forma en el caso de las arterias aberrantes.

Los autores estudian también la irrigación sanguínea en el riñón en herradura y en el riñón discoidéo, así como en la pelvis, cálices y uréter. También el autor subraya la importancia del hazar quirúrgico de encontrar en el curso de la cirugía un arco gonadal arterial (16%) en el pedículo renal.

La multiplicidad las arterias renales se

explica desde el punto de vista embriológico, ya que las variaciones encontradas son restos de las arterias dejeneradas parcialmente del mesonefros primitivo. Sobre la base de la literatura mundial referente a la irrigación sanguínea del riñón se ha logrado demostrar muchos conceptos anatomoclinicopatológicos tales como el mecanismo de los atajos medulares de Trueta, las posibles rutas de la circulación colateral en el riñón y la esquemia renal en sus relaciones con la hipertensión primaria y con la insuficiencia renal aguda. Se discuten finalmente las nuevas imágenes anatomoradiológicas con amplia referencia a la importancia de los arteriogramas renales en el preoperatorio.

RIASSUNTO

Su 185 cadaveri di adulti è state studiata la vascolarizzazione del rene. In 50 furono studiate anche le arterie surrenali e le diaframmatiche inferiori, su pezzi anatomici che rappresentavano tutta la regione asportata in blocco e preparata nei più minuti particolari. I risultati dello studio sono stati confrontati con tutto quanto è stato scritto in materia negli ultimi 75 anni, e precisamente con 150 lavori letti e riassunti per esteso.

La vascolarizzazione del surrene è così variabile che non è possibile trovare due casi uguali e neppure l'uguaglianza fra i due lati nello stesso individuo. Non è vero che essa sia rappresentata da tre arterie principali, come si sostiene da cento anni a questa parte in ogni trattato; comprende invece: 1) da 4 a 30 arterie superiori delle dimensioni di ramuscoli, che provengono o dalla diaframmatica inferiore o dal suo ramo posteriore; 2) da un'arteria media, proveniente dall'aorta, incostante; 3) da un'arteria inferiore, il più spesso unica e derivante dalla renale, altre volte multipla e di varia origine (aorta, a. renale, polare superiore, capsulare). Il sistema arterioso surrenalico è poi in intimi rapporti con quello del rene, dacchè i rami arteriosi della capsula adiposa danno spesso origine alla surrenale inferiore, mentre questa a sua volta può dare rami polari o capsulari.

Dallo studio statistico di 11.000 reni riferiti dalla letteratura e di 185 preparazioni anatomiche personali l'autore conclude che l'arteria renale è unica nel 72%, duplice nel 10%, tripla o quadrupla raramente. Le arterie polari superiori provengono dall'aorta nel 7% dei casi e dalla renale nel 12%; la frequenza delle prime è del 5,5%, quella delle seconde dell'0,4% sul totale dei casi.

Graves, di Londra, ha dimostrato recentemente per mezzo di iniezioni che il rene è un organo diviso in segmenti come il polmone e il fegato; tali segmenti sono cinque: l'apicale, il superiore, il medio, l'inferiore e il posteriore. Basandosi su questi dati, l'autore ha confermato con il suo materiale l'ipotesi di Graves e cioè che il disegno arterioso renale è sempre costante indipendentemente dall'origine delle arterie. Anche le arterie renali accessorie (aberranti) devono essere considerate normali allo stesso modo come le cosidette arterie accessorie epatiche e dotti accessorii epatici. Dal punto di vista anatomico e funzionale la legatura di ogni arteria renale, così come di ogni arteria aberrante, produce la necrosi della zona rifornita.

Per finire viene trattata la vascolarizzazione dei reni a ferro di cavallo e di quelli a disco, della loro pelvi, calici e ureteri; viene anche sottolineata l'importanza chirurgica della presenza, così frequente (16%) di un'ansa dell'arteria spermatica nel peduncolo renale.

La molteplicità delle arterie renali è interpretata su una base embriologica, nel senso che le varianti incontrate rappresentano arterie del mesonefros persistenti integralmente o in parte.

Su questi studi si possono fare delle illa-

zioni di carattere anatomo-patologico e clinico, fra cui il corto circuito midollare di Trueta, le eventuali vie collaterali del rene, l'ischemia renale e i suoi rapporti colla ipertensione primitiva e coll'insufficienza acuta del rene.

RÉSUMÉ

L'apport sanguin variable du rein a été étudié au cours de 185 dissections de reins provenant d'adultes. L'artère rénale et l'artère phrénique inférieure ont été examinées sur 50 cadavres (toute la région environnante a été prélevée en bloc). Les auteurs ont fait l'étude comparative la plus importante jusqu'à ce jour avec la littérature mondiale des 75 dernières années.

L'apport sanguin varie à un point tel qu'il n'est jamais semblable d'un sujet à l'autre, ni même d'un côté à l'autre du même sujet. Il ne s'effectue pas par trois troncs artériels comme l'affirment les manuels depuis plus de 100 ans, mais il englobe: 1) de 4 à 30 petits vaisseaux rénaux supérieurs dérivant du tronc phrénique inférieur, ou de sa division postérieure; 2) un vaisseau médian provenant en majorité de l'aorte, mais souvent absent et remplacé par une autre artère; 3) un vaisseau inférieur, surtout d'origine rénale seule, mais souvent d'origine multiple et variée (aorte, branche rénale polaire supérieure). L'apport sanguin adrénalien est intimement lié à celui du rein, car la branche adipeuse capsulaire allant au rein donne fréquemment naissance à une branche suprarénale inférieure. Cette dernière, à son tour, peut émettre des vaisseaux polaires rénaux et des branches capsulaires.

Il a été conclu, de l'étude statistique de 11.000 reins rapportés dans la littérature et des 185 dissections effectuées par les auteurs, que l'artère rénale est unique dans 72% des cas, et double dans 10% des cas. Il existe en fait des artères rénales triples ou même quadruples, mais c'est l'exception. Les artères polaires supérieures proviennent de l'aorte dans 7% des cas, et de l'artère rénale dans 12% des cas. Les artères aortiques polaires inférieures se présentent dans une proportion de 5,5%, les artères rénales dans 1,4%.

Graves, de Londres, a récemment démontré au moyen de moulages plastiques que la rein est un organe segmentaire, tout comme le poumon et le foie. Les segments du rein se divisent en: apical, supérieur, médian, inférieur et postérieur. Les observations des auteurs leur permettent de confirmer l'affirmation de Graves, à savoir que le type artériel à l'intérieur du rein est constant, indépendamment de l'origine variable de l'artère segmentaire.

Comme les soi-disant artères hépatiques accessoires et les conduits hépatiques "accessoires," les artères rénales accessoires (aberrantes) sont des structures normales. Des points de vue anatomique et fonctionnel, elles naissent du tronc rénal, de l'aorte ou d'une autre source, et la section d'une artère rénale quelconque produit une nécrose dans la zone qu'elle alimente, comme c'est le cas lors de la section d'une artère aberrante.

Les auteurs décrivent également l'apport sanguin du rein en fer à cheval et du rein en galette, ainsi que celui du bassinet, des calices et de l'uretère. Le risque chirurgical de la "gonadal artery" voussée qui est fréquente (16%) dans le pédicule rénal, est souligné. La multiplicité des artères rénales est expliquée embryologiquement, les variétés rencontrées étant des vestiges complets ou des artères primitives mésonéphriques en partie dégénérées. De nombreuses considérations anatomo-clinico-pathologiques sont présentées sur la base de la littérature mondiale concernant l'apport sanguin rénal, telles que le mécanisme du conduit de dérivation médullaire de Trueta, les voies possibles de la circulation collatérale au rein, avec un essai d'analyse englobant aussi l'ischémie rénale et

son rapport avec l'hypertension primaire, et la défaillance rénale aiguë. Le nouveau tableau radiologique des artères rénales est discuté, et de nombreuses références sont faites quant à la signification chirurgicale pré-opératoire des artériogrammes rénaux.

ZUSAMMENFASSUNG

Die verschiedenen Formen der Blutversorgung der Nieren wurden an 185 Nierenpräparaten von Leichen Erwachsener im Seziersaal untersucht. Die Nebennierenarterien und die A. phrenica inf. wurden an 50 Leichen untersucht, bei denen die gesamte in Frage kommende Gegend *en bloc* reseziert und dann im Einzelnen auspräpariert wurde. Die Verfasser verglichen ihre Beobachtungen in einer bisher niemals durchgeführten umfassenden Weise mit den in der Weltliteratur der letzten 75 Jahre berichteten Ergebnissen. Ihre Studium erstreckt sich auf etwa 150 Arbeiten, die sie sorgfältig gelesen und angeführt haben.

Die Blutversorgung der Nebennieren ist so wechselnd, dass in zwei Leichen oder auch in beiden Seiten desselben Körpers niemals die gleiche Form vorkommt. Die Blutversorgung erfolgt nicht, wie seit über 100 Jahren in den Lehrbüchern behauptet wird, durch drei einzelne Stammarterien, sondern (1) durch 4 bis 30 obere Nebennierenäste, die aus dem Stamm oder der hinteren Abzweigung der A. phrenica inf. kommen, (2) durch ein mittleres Nebennierengefäss, das vorwiegend von der Aorta stammt, aber häufig nicht vorhanden ist oder durch eine andere Arterie ersetzt wird, und (3) durch ein unteres Nebennierengefäss, das meistens als einzelne Ader aus der Nierenarterie entspringt, aber in vielen Fällen auch in der Mehrzahl vorkommt und aus verschiedenen Quellen (Aorta, Nierenarterie, Ast für den oberen Nierenpol oder für die Nierenkapsel) stammt. Die Blutversorgung der Nebenniere steht zu dem der Niere in enger Beziehung, da der die Fettkapsel der Niere versorgende Ast häufig eine untere Nebennierenschlagader abgibt. Diese andererseits kann Äste zum Nierenpol oder zur Nierenkapsal aussenden.

Eine auf 11 000 in der Literatur veröffentlichte und auf 185 von den Verfassern untersuchte Nierenpräparate sich stützende statistische Untersuchung führt zu der Schlussfolgerung, dass in 72 Prozent der Fälle die Nierenarterie einzeln und in 10 Prozent der Fälle doppelt vorkommt. Dreifache und vierfache Nierenarterien treten nur selten auf. Obere Nierenpolarterien entspringen in 7 Prozent der Fälle von der Aorta und in 12 Prozent von der Nierenarterie. Untere aus der Aorta stammende Nierenpolarterien kommen in 5,5 Prozent, aus der Nierenarterie stammende in 1,4 Prozent vor.

Graves (London) hat an Hand von aus Kunststoffen bestehenden Ätzpräparaten kürzlich nachgewiesen, dass die Niere ähnlich wie die Lunge und die Leber ein Lappenorgan ist. Sie besteht aus einem Spitzenlappen, einem oberen, mittleren, unteren und hinteren Lappen. Die Verfasser verglichen diese Feststellung mit ihren Befunden über den Verlauf der Nierenarterien und bestätigten Graves' Auffassung, d. h. dass der Gefässverlauf innerhalb der Niere ohne Rücksicht auf die Verschiedenheit des Ursprungs der Lappenarterie konstant ist. Akzessorische (von der gewöhnlichen Form abweichende) Nierenarterien sind wie die sogenannten akzessorischen Leberarterien und "akzessorischen" Lebergänge normale Gebilde. Vom anatomischen und funktionellen Gesichtspunkt aus betrachtet entspringen sie vorzeitig aus dem Stamm der Nierenarterie, aus der Aorta oder aus einer andern Quelle. Ihre Durchtrennung führt wie bei jeder Nierenarterie zur Nekrose des Abschnittes, den sie versorgt.

Es wird ferner über die Blutversorgung der Hufeisenniere, der diskusförmigen Niere, des Nierenbeckens, der Nierenkelche und der Harnleiter berichtet. Hervorgehoben wird das chirurgische Risiko, das mit dem häufigen (16%) Vorkommen der bogenförmigen zu den Geschlechtsdrüsen führenden aus der Nierenwurzel stammenden Arterie einhergeht. Die Multiplizität von Nierenarterien wird auf embryologischer Grundlage erklärt. Die beobachteten Abweichungen stellen völlig erhalten gebliebene oder teilweise degenerierte primitive Urnierenarterien dar. Auf Grund der Berichte über die Blutversorgung der Niere in der Weltliteratur werden viele anatomisch-klinisch-pathologische Zusammenhänge erklärt, z. B. Truetas medullärer Umgehungsmechanismus, die möglichen Wege und die angestellten Versuche zur Herstellung eines Kollateralkreislaufs der Niere, Nierenischämie und ihre Beziehung zur primären Hypertonie und zur akuten Anurie. Die neuen röntgenologischen Darstellungen der Anatomie der Nierenarterien werden unter Hinweis auf die präoperative Bedeutung des Nierenarteriogramms erörtert.

## BIBLIOGRAPHY

Adachi, B.: Das Arteriensystem der Japaner. Tokyo: Kenkyusha Press, 1928, 2 vols. Venensystem der Japaner. Tokyo: Kenkyusha Press, 1940, 1 vol.

Albarran, J.: Médicine operatoire des voies urinaires. Paris: G. Mason et Cie., 1909.

Albarran, J., and Papin, E.: Anatomie du bassinet et l'exploration sanglante du rein, Rev. d. Gynec. & chir. abdom. 12:215, 1908.

Ancel, P.: Cited by Iglesias, 1909 Documents recueilles a la salle de dissection de la faculté de medicine de Nancy, Bibliog. anatom. vols. 9 and 12, 1901-1903.

Anson, B. J.: Atlas of Human Anatomy. Philadelphia: The W. B. Saunders Company, 1950.

Anson, B. J.; Cauldwell, E.; Pick, J., and Beaton, L.: The Blood Supply of the Kidney Suprarenal Gland and Associated Structures, Surg. Gynec. & Obst. 84:313, 1947. The Anatomy of the Pararenal System of Veins, with Comments on the Renal Arteries. J. Urol. 60:714, 1948.

Anson, J. B., and Kurth, L.: Common Variations in the Renal Blood Supply, Surg., Gynec. & Obst. 100:156, 1955.

Anson, B. J., and McVay, C.: The Topographical Positions and the Mutual Relations of the Visceral Branches of the Abdominal Aorta, Anat. Rec. 67:7, 1936.

Anson, B. J.; Pick, J., and Cauldwell, E.: The Anatomy of the Commoner Renal Anomalies; Ectopic and Horseshoe Kidneys, J. Urol. 47:112, 1942.

Anson, J. B.; Richardson, G., and Minear, W.: Variations in the Number and Arrangement of the Renal Vessels, J. Urol. 36:211, 1936.

Balint, J., and Palkovich, I.: The Intrarenal Relation of Abnormal Kidney Arteries to the Renal Artery, Magyar Sebészet, 5-6:131, 1952-1953.

Batson, O. V.: The Function of the Vertebral Veins and Their Role in the Spread of Metastases, Ann. Surg. 112:138, 1940.

Bell, E. T.: Renal Diseases. Philadelphia: Lea and Febiger, 1946.

Bonney, C. W.: Studies in the Anatomy of The Kidney, Am. J. Urol. 8:607, 1912.

Botez, G.: Considérations sur la pathologie et la chirurgie du rein en fer a cheval, J. d. urol. 1:193, 1912.

Boyden, E. A.: Description of a Horseshoe Kidney Associated with Left Inferior Vena Cava and Disc-Shaped Suprarenal Glands, Together with a Note on the Occurrence of Horseshoe Kidneys in Human Embryos, Anat. Rec. 51:187, 1932.

Bremer, J. L.: The Origin of the Renal Artery in Mammals and Its Anomalies, Am. J. Anat. 18:178, 1915.

Brewer, G. E.: Some Observations upon the Anatomy of the Kidney, N.Y. M. News 71:129, 1897.

Brödel, M.: The Intrinsic Blood-Vessels of the Kidney and Their Significance in Nephrotomy, Bull. Johns Hopkins, Hosp. 12:10, 1901.

Broman, I.: Über die Entwickelung und Wanderung der Zweige der Aorta abdominalis beim Menschen, nebst Bemerkungen über Gefässwurzelwanderungen in Allgemeinen, Anat. Hefte 1. Abteil. 110:406-450, 1908. Die Entwickelung des Menschen vor der Geburt. Munich: J. F. Bergman, 1927.

Busch, W.: Die arterielle Gefässversorgung der Nebennieren (zugleich ein Beitrag zur Anatomie der Nierenarterien), Virchow's Arch. f. path. Anat. u. Physiol. 324:688, 1954.

Capolare, L.: Contributo alla studio dell'idonefrosi con vasi anomali, Arch Ital. di chir. 24:503, 1929.

Carlau, F.: Die Anomalien der Nirenarterien, Inaug. Dissert. Kiel, 1893.

Carson, W. J.: Anomalous Renal Vessels and Their Surgical Significance, West. J. Surg. 40:597, 1932.

Cauldwell, E. W., and Anson, B. J.: The Visceral Branches of the Abdominal Aorta; Topographical Relationships, Am. J. Anat. 73:27, 1943.

Cordier, P.; Devos, L.; Delcroix, A., and Renier, M.: Variations du trajet de l'artère spermatique, Ann. anat. path. Paris 15:535, 1938.

Daniel, O., and Shackman, R.: The Blood Supply of the Human Ureter in Relation to Ureterocolic Anastomosis, Brit. J. Urol. 24:334, 1952.

Davis, H. C., and Morse, I. S.: Renal Revascularization by Splenic Artery Implantation, Arch. Surg. 75:13, 1957.

Dees, J. E.: Congenital Anomalies of the Upper Urinary Tract, J. Urol. 46:659, 1941.

Dege, H. A.: Zur Bedeutung der unteren Nierenpolgefässe, Ztschr. f. Urol. 33:385, 1939.

Doss, A. K.: Translumbar Aortography; its Diagnostic Value in Urology, J. Urol. 55:594, 1946.

Douville, E., and Hollinshead, W. H.: The Blood Supply of the Normal Renal Pelvis, J. Urol. 73:906, 1955.

Duff, G. L., and More, R. H.: Methods of Preparation and Examination of Neoprene Casts of the Renal Arterial Tree, J. Tech. Methods 24:1, 1944.

Edsman, G.: Accessory Vessels of the Kidneys and Their Diagnosis in Hydronephrosis, Acta. Radiol. 42:26, 1954.

Eisendrath, D. N.: The Relation of Variations in the Renal Vessels to Pyelotomy and Nephrectomy, Ann. Surg. 71:726, 1920. Hydronephrosis Due to Obstruction of the Renal Pelvis by One of the Two Main Renal Arteries, J. Urol. 24:173, 1936.

Eisendrath, D. N., and Strauss, D. S.: The Surgical Importance of Accessory Renal Arteries, J.A.M.A. 55:1375, 1910.

Ekelhorn, G.: Die anormalen Nierengefässe und die Hydronephrose, Fol. Urol. 1:755, 1908.

Ekehorn, G.: Zur Behandlung der durch anormale Nierengefässe verursachten Hydronephrose, Ztschr. f. urol. Chir. 10:122, 1922.

Fagarasanu, I.: Recherches anatomique sur la veine rénale gauche et ses collatérales. Leurs rapports avec la pathogénie du varicocèle essentiel et des varices du ligament large, Ann. d'anat. path. med. chir. 15:9-52, 1938.

Felix, W.: The Development of the Urogenital Organs. In Keibel, and Mall, Human Embroyology. Philadelphia: The J. B. Lippincott Company. vol. 2. p. 822.

Fetter, T. R.: Renal Vascular Anomalies and Renal Disease, Pennsylvania Med. 34:324, 1931.

Fetter, T. R.; Varano, N. R., and Ayres, R. D.: Horseshoe Kidney. Scientific Exhibit, Chicago June 11-15, 1956.

Fishberg, A.: Hypertension and Nephritis. Philadelphia: Lea and Febiger, 1931.

Fitel, A.: Cited by Michaels (1895).

Gérard, G.: Les anomalies congénitales du rein chez l'homme. Essai de classification d'après 527 cas. J. d. l'anat. et physiol. 41:410-39, 1905. Les artères renales (Note statistique d'après l'étude de 150 paires de reins, ibid. 47:531, 1911. Sur les variations d'origine et de nombre des artères genitales, spermatique ou ovarienne de l'homme, Compt. rend. soc. biol. 74:778, 1913. Contribution à l'étude morphologique des artères des capsules surrenales de l'homme, J. d'anat et d. Physiol. 49:269, 1913.

Gérard, G., and Castiaux, P.: Sur les territoires artèriels du rein de quelques mammifères et de l'homme, Compt. rend d'assoc. d'anat. 5:208, 1903.

Gillaspie, C.; Miller, L., and Baskin, M.: Anomalous Renal Vessels and Their Surgical Significance, Anat. Rec. 11:77, 1916.

Golubev, A.: Zur chirurgischen Anatomie der Nierenarterien. Ztschr. f. urol. Chir. 21:307, 1927.

Graves, F. T.: The Anatomy of the Intrarenal Arteries and Their Application to Segmental Resection of the Kidney, Brit. J. Surg. 42:132, 1954. The Aberrant Renal Artery, J. Anat. 90:553, 1956.

Greig, H. W.; Anson, B. J., and Coleman, S. S.: The Inferior Phrenic Artery: Types of Origin in 850 Body-Halves and Diaphragmatic Relationship, Quart. Bull. Northwestern Univ. M. School 25:345, 1951.

Grant, J. C.: In Boileau: Method of Anatomy: Atlas of Anatomy. Baltimore: Williams and Wilkins, 1951.

Gray, G. M.: Multiple Renal Arteries, Anat. Anz. 29:266, 1906.

Gutierrez, R.: The Clinical Management of Horseshoe Kidney. New York: Paul B. Hoeber, Inc., 1934.

Heidsieck, E.: Zur Skeletotopie der grossen Aste der Bauchaorta, Anat. Anz. 66:6, 1928.

Hellström, J.: A Contribution to the Knowledge of the Relation of Abnormally Running Renal Vessels to Hydronephrosis and an Investigation of the Arterial Conditions in 50 Kidneys, Acta. chir. Scand. 61:289, 1927. Zur Kenntniss der Doppelnieren, Ztschr. f. urol. Chir. 23:31, 1927. Über die Varianten der Nierengefässe, ibid. 24:253, 1928. Beitrag zur Behandlung der infolge von Ureterkompression durch Nierengefässe entstandenen Hydronephrose, ibid. 39:160, 1934.

von Helm, F.: Zur Topographie der menschlichen Nieren, Anat. Anz. 11:97, 1895.

Herman, J. L., and Fetterolf, G.: "Dumb-bell" Kidney, Ann. Surg. 57:868, 1913.

Hollinshead, W. H.: Anatomy for Surgeons. New York: Paul B. Hoeber, Inc., 1956, vol. 2.

Hou-Jensen, H. M.: Die Verästelung der Arteria renalis in der Niere des Menschen, Ztschr. f. Anat. u. Entwick. 91:1-129, 1930.

Hughes, A.: Abnormal Arrangement of Arteries in the Region of the Kidney and Suprarenal Body, J. Anat. & Physiol. 26:305, 1892.

Iglesias, A. E.: Les anomalies des artères du rein. These, Paris, 1909.

Iijima, H.: Lageverhalten der A. und V. renalis und des Ureters der Japaner, Tokyo-Iji-Shinshi. No. 2415, 1925 (cited by Adachi).

Iwanow, G.: Über die Lagebeziehungen der Nieren und Nebennieren beim Menschen, Anat. Anz. 64:163, 1927.

Jeanneney, G., and Massé, L.: Anomalies des artères du rein. (Étude radiographique des territoires artèriels) J. d'. Med. d'. Bordeaux 49:117, 1920.

Jeidell, H.: A note on the Source and Character of the Blood Vessels of the Kidney, Anat. Rec. 5:47, 1911.

Jewett, H. J.: Accessory Renal Vessels: Their Influence in Certain Cases of Hydronephrosis, Surg., Gynec. & Obst. 68:666, 1939.

Johnstone, P.; Stone, R.; Burdick, H.; Allebach, H.; Patton, L; Tuller, F., and Erb, L.: Studies on the Etiology and Treatment of Acute Renal Failure, J.A.M.A. 161:491, 1956.

Kolster, R.: Studien über die Nierengefässe, Ztschr. f. Morph. u. Anthrop. 4:179, 1902.

Kubo, T.: Über die Varietäten der A renalis, Tokyo-Igakkwai-Zasshi 21:613, 1907 (cited by Adachi).

Lapeyre, J. L.: Anomalies des artères renales et rein en fer a cheval, Ann. d'Anat., Pathol., Med., Chir. 6:853, 1929.

Legueu, F., and Papin, E.: Le rein en fer a cheval. Étude anatomique, pathologique et chirurgicale, Rev. d. Gynec. e d. chir Abdom. 18:277, 1912.

Levi, G.: Le variazioni delle arterie surrenali e renali studiate col metodo statistico seriale, Arch. Ital. Anat. e d. Embrio 8:35, 1909. Ref. in Schwalbe's Jahresberichte 15:304, 1909.

Lipshutz, B., and Hoffman, S.: A Contribution to the Knowledge of Fused Kidneys, Ann. Surg. 67:39, 1918. Renal Arterial Variations and Extraperitoneal Abdominal Nephrectomy, ibid. 81:525, 1926.

Lloyd, L. W.: Renal Arteries in Whites and American Negroes, J. Phys. Anthropol. 20:153, 1935.

Loth, E.: Anthropologie des parties molles: Foundation, Mianowski, Varsovie, Paris, 1930.

Lowsley, O. S.: Surgery of the Horseshoe Kidney, J. Urol. 67:565, 1952.

Luna, E.: Sulla irrorazione arteriosa delle glandole soprarenali dell'uomo Ric. fatte nel Lab. di Anat. Norm. dell R. Univ. di Roma 14:145, 1908, Ref. Merkel-Bonnets Ergebnisse 19:442, 1909.

Macalister, A.: Multiple Renal Arteries, J. Anat. & Physiol. 17:250, 1883.

Martin, K.: Ungewöhnlicher Verlauf einer arteria suprarenalis, Acta Anat. 24:48, 1955.

Mayo, W. J.; Braasch, W. F., and MacCarty, W. C.: Relation of Anomalous Renal Blood Vessels to Hydronephrosis, J.A.M.A. 52:1383, 1909.

Mazza, E.: Ricerche anatomische sulle arterie surrenali dell'uomo, Minerva chir. 9:175, 1954. Note di anatomia chirurgica appunti di anatomia delle arterie renali nell'uomo, ibid. 9:738. 1954.

Melkonian, L.: Systematisation de 44 cas d'anomalie des artères renales, Acta med. Jugoslavica 8:257, 1954.

Michaels, J. P.: Study of Ureteral Blood Supply and Its Bearing on Necrosis of the Ureter Following the Wertheim Operation, Surg., Gynec. & Obst. 86:36, 1948.

Michels, N. A.: Blood Supply and Anatomy of the Upper Abdominal Organs, with a Descriptive Atlas. Philadelphia: The J. B. Lippincott Company, 1955.

Miyashita, K.: Über die Nierenarterie bei Chinesen, J. Oriental Med. (Abstr.) 23:21, 1935.

Moody, R., and Van Nuys, R.: The Position and Mobility of the Kidneys in Healthy Young Men and Women, Anat. Rec. 76:111, 1940.

More, R. H., and Duff, G. L.: The Renal Arterial Vasculature in Man, Am. J. Path. 27:95, 1951.

Morison, D. M.: A Study of the Renal Circulation, with Special Reference to its Finer Distribution, Am. J. Anat. 37:53, 1926.

Nañagas, J. C.: Position and Size of the Kidneys among Filipinos, Philippine J. Science 18:695, 1921.

Nelson, O. A.: Arteriography in Renal and Abdominal Conditions, J. Urol 53:521, 1945.

Notkovich, H.: Variations of the Testicular and Ovarian Arteries in Relation to the Renal Pedicle, Surg. Gynec. & Obst. 103:497, 1956.

Papin, E.: Chirurgie du rein. Paris: G. Doin et cie., 1928.

Petren, G.: Beiträge zur Frage von der klinischen Bedeutung der akzessorischen Nierengefässe, Beitr. z. klin. Chir. 125:493, 1921. Eine wie grosse Rolle spielen abnorme Nierengefässe als Ursache von Hydronephrose resp. Pyonephrose?, Ztschr. f. Urol. 28:145, 1934.

Pick, J. W., and Anson, B. J.: The Renal Vascular Pedicle, J. Urol. 44:411, 1940. The Inferior Phrenic Artery: Origin and Suprarenal Branches, Anat. Rec. 78:413, 1940.

Pohlman, A.: A Note on the Developmental Relation of the Kidney and Ureter in Human Embryos, Bull. Johns Hopkins Hosp. 16:49, 1905. Abnormalities in the Form of the Kidney and Ureter Dependent on the Development of the Renal Bud, ibid. 16:51, 1905. Concerning the Embryology of the Kidney Anomalies, Am. Med. 7:987, 1904.

Poynter, C. W.: Congenital Anomalies of the Arteries and Veins of the Human Body, with Bibliography. Nebr. Univ. Studies, Lincoln, 22: 1-106, 1923.

Priman, J.: A Consideration of Normal and Abnormal Positions of the Hilum of the Kidneys, Anat. Rec. 42:355, 1929.

Quevedo, A. G. de: Variations en la distribusion y numero de los vasos del rinon. Estudio de diseccion y corrosion de los rinones, Gaseta Med. de Mexico 78:53, 1948.

Ribeiro, O.: Cited by Dos Santos, R., Fol. Anat. Univ. Conimb. 5:1-14, 1930.

Riches, E. W.: The Present Status of Renal Angiography, Brit. J. Surg. 42:462, 1955.

Robinson, B.: The Blood Vessels in Fused (Horseshoe) Kidney, Based on the Study of Sixty Specimens and Illustrations, Lancet 1:141, 1909.

Ronstrom, G. N.: Incidence of Single and Multiple Renal Arteries in Negroes, Am. J. Phys. Anthropol. 5:485, 1947.

Rousseau, P.: Anomalies des artères du rein. Thèse, Paris, 1894. Cited by Levi, and by Jeanneney and Massé.

Rupert, R. R.: Irregular Kidney Vessels Found in Fifty Cadavers, Surg, Gynec. & Obst. 17:580, 1913.

Rupert, R. R.: Further Study of Irregular Kidney Vessels as Found in One Hundred Eighteen Cadavers, Surg. Gynec. & Obst. 21:471, 1915.

Santaelia, R. R.: Alcunas consideraciones sobre las anomalias de las arterias renales y su importancia en cirugia, Arch. d. Med., Chir. y Espec. 27:66, 1927.

dos Santos, R.: Sur la multiplicite des artères renales, Fol. Anat. Univ. Conimb. 5:1-14, 1930.

dos Santos, R.; Lamas, A., and Caldas, J. P.: Arteriografia da aorta e dos vasos abdominais, A. Medicina Contemporanea 47:93, 1929.

Schmerber, F.: Recherches anatomiques sur l'artère renal. Thèse, Lyon, 1895, cited by Hellström.

Seldowitsch, J. B.: Über die Multiplicität der Nierenarterie und deren chirurgische Bedeutung, Arch. f. klin. Chir. 89:107, 1909.

Smithuis, T.: The Problem of Renal Segmentation in Connection with the Modes of Ramification of the Renal Artery and Renal Vein, Arch. Chir. Neerlandi 8:3, 1956.

Smirnoff, J. M.: Über Variation von Nierengefässen die chirurgische Bedeutung haben. Ref. in Zentralorgan f. d. ges. Chir. u. ihre Grenzg. 15:446, 1922.

Spanner, R.: Über Gefässkurzschlüsse in der Niere, Verh. d anat. Gesellsch. 45:81, 1937-1938.

Swinyard, C. A.: Volume and Cortico-medullary Ratio of the Adult Human Suprarenal Gland, Anat. Rec. 76:69, 1940.

Thane'. Quain's Elements of Anatomy (10th ed.) London, 1882. Cited by Levi.

Thomson, A.: Report of the Committee of Collective Investigation of the Anatomical Society of Great Britain and Ireland, for the Year 1889-1890, J. Anat. & Physiol. 25:89, 1891.

Thorek, P.: Anatomy in Surgery. Philadelphia: The J. B. Lippincott Company, 1951.

Taniguchi, T.: Beitrag zur Topographie der grossen Aste der Bauch aorta, Fol. anat, Japonica 9:201, 1930-1931.

Trueta, J.; Barclay, A.; Daniel, P.; Franklin, K., and Prichard, M.: Studies of the Renal Circulation. Springfield, Ill.: Charles C Thomas, Publisher, 1947.

Wagner, F. B.: Arteriography in Renal Diagnosis, J. Urol. 56:625, 1946.

Wagner, F. B.; Price, A. H., and Swenson, P. C.: Abdominal Arteriography; Technique and Diagnostic Application, Am. J. Roent. 58:591, 1947.

Walters, W.: The Conservative Treatment of Hydronephrosis by Resections of the Renal Pelvis and Other Plastic Operations, J. Urol. 29:121, 1933.

Weinstein, B.; Countiss, E., and Derbes, V.: The Renal Vessels in 203 Cadavers, Urol. Cutan. Rev. 44:137, 1940.

Westerborn, A.: Über Nierentorsion und abnorm verlaufende Nierengefässe, Arch. chir. Scand. 68:25, 1931.

Winsbury-White, H. P.: Observations on Hydronephrosis, with Special Reference to Aberrant Vessels, Tr. Am. A. Genito.-Urin. Surg. 29:381, 1936.

Young, A. H., and Thompson, P.: Abnormalities of the Renal Arteries, with Remarks on Their Development and Morphology, J. Anat. & Physiol. 38:1, 1903.

Preparation for a patient who will be left with a colostomy requires . . . forethought. A way to handle the problem is to inform the patient before the operation that he may be left with an abdominal anus, that this may be a temporary opening (the impression is left that it is usual to keep the colostomy open for six months), and that at the end of such period the decision will be made as to whether normal bowel continuity can be restored. When the patient is in the early days of his colostomy, which are rugged days for him, he bears them better with the thought that this is a temporary expedient. He is taught how to use the irrigating apparatus, he finds that he can go out into society with safety, and as the end of the six months approaches he becomes less and less insistent in his questions about restoration . . . Man is so adaptable that caring for a colostomy becomes just another routine for him; in time he will carry on his activities with little consciousness of an infirmity.

—*Standard*

# Use of Radioactive Colloidal Chromic Phosphate for Prevention of Amputation Neuroma*

JOHN I. PERL, M.D., F.A.C.S.
CHICAGO, ILLINOIS
AND
DAVID G. WHITLOCK, M.D.
SYRACUSE, NEW YORK

THE proximal stump of a divided nerve, when permanently separated from its distal segment, heals with a scar whose size, shape and bulk are determined by a multitude of conditions existing in the surrounding tissues during the healing process. In amputated extremities the nerve stumps will often heal with large bulbous scars, commonly known as amputation neuromas.

Amputation neuromas are not true tumors. On histologic examination they appear as disorganized masses of connective tissue and Schwann cells into which bundles of axis cylinders have penetrated in a haphazard manner. While the connective tissue elements of the scar tend to contract, the neuroplasm of the individual nerve fiber may continue its proximodistal growth as long as the centrally located cell body continues to manufacture neuroplasm. As a result, a struggle exists between the constricting force of the shrinking fibrous tissue and the increasing pressure of the expanding neuroplasm in the severed nerve fiber.

This disorganized growth in the neuroma does not necessarily impair the conduction properties of the nerve fibers involved. On the contrary, the ballooning, beading and telescoping of these terminal deformities may lower the threshold of the afferent fibers to the point where previously subliminal stimuli may begin to discharge spontaneously and produce an intense sensory barrage.

This input from the nerve stump to the central nervous system would be relayed, in part, to the sensory receiving areas of the thalamus and the cerebrum. Certain regions of the latter are known to have a detailed relation to sensory structures of parts of the body so that a "point-to-point" type of projection exists.[1] Thus, activity in neurons of these projection regions, whether evoked from an intact sense organ or by discharge from an injured afferent fiber, would result in similar interpretive or reflex events, the source of which could not be distinguished. This organization may form the basis of a mechanism for apparent sensation in a nonexistent limb and

From the Department of Surgery, Augustana Hospital, Chicago (Dr. Perl), and the Department of Anatomy, College of Medicine, State University of New York, Syracuse (Dr. Whitlock).
*Supported in part by research grant B-1182 from the National Institute of Neurological Diseases and Blindness, Public Health Service, and in part by a research grant from the Nelson M. Percy Medical Research Foundation, Augustana Hospital, Chicago.
Submitted for publication Oct. 16, 1957.

is not difficult to understand in the light of current anatomic and neurophysiologic concepts. There is evidence indicating that a continuous high level of activity in sensory fibers facilitates synaptic activation of neurons in the central nervous system for considerable periods.[2] It is possible, therefore, that once a painful phantom limb has been established by aberrant activity in the axons of a neuroma, it may persist after removal of the initiating source.

The intractable, painful phantom and its presumed association with the scar of the severed nerve prompted surgeons to use a variety of procedures to prevent the development of amputation neuromas. Nerve stumps were sectioned, ligated, implanted into muscle and bone, capped with plastic resins, injected with chemical agents, electrodesiccated, cauterized, coagulated and quick-frozen. In certain instances several of these procedures were used in combination.[3]

The effectiveness of a given procedure was judged according to the presence or absence of pain in the healed stump. However, the incidence of painful stump is comparatively low, which makes the clinical evaluation of prophylactic procedures unreliable. On the other hand, Pinto and Junqueira[4] showed that in the overwhelming majority of rats histologically verified neuromas developed in the following circumstances:

1. Simple section, with or without ligation of the nerve.

2. Section and ligation of the nerve, plus the application of a collodion cuff over the stump.

3. Injection of the ligated nerve with (a) alcohol, (b) solution of formaldehyde and (c) gentian violet.

Typical neuromas developed in 77 to 100 per cent of the animals under these experimental conditions. The incidence of neuromas was reduced to 50 per cent when Methods 2 and 3 in combination were supplemented by the application of powdered tannic acid to the divided nerve.

It would appear that one or both of the following facets of neuroma formation must be influenced if prophylaxis is to be accomplished: First, synthesis of neuroplasm must be inhibited in the centrally located cell bodies of the amputated axons, and second, a *sustained inhibitory effect* must be achieved, either upon the regeneration of the fibroblasts or the Schwann cells or upon the biochemical and enzymic process that regulates the metabolism of the neuroplasm in the stump of the amputated nerve.

The likelihood of abolishing neuroplasm synthesis at the perikaryon level is not encouraging, since the position of the cell bodies in the dorsal root ganglia and in the anterior horn of the spinal cord preclude a direct attack upon them. Furthermore, no safe and selective neurotoxin is available which, applied to the peripheral nerve, would ascend centrally and confine its effects to the corresponding cell bodies of the involved axons or dendrites. This restricts prophylaxis to the nerve trunk proper and to its proximal stump.

The present study was undertaken to discover and evaluate new substances which might inhibit the growth of nerve elements in the proximal stump of a divided peripheral nerve.

*Material and Methods (Animal Experiments).* — Rats 3 to 4 months old were anesthetized intraperitoneally with 4 mg. of nembutal sodium per hundred grams of body weight. They were shaved; the skin was prepared with tincture of Mercresin; and both sciatic nerves were exposed between the gluteal muscles at the trochanteric level. Approximately 1 cm. of each nerve was resected. The proximal stump of the right sciatic nerve was ligated with fine cotton thread and was utilized as the control in each animal. The stump of the

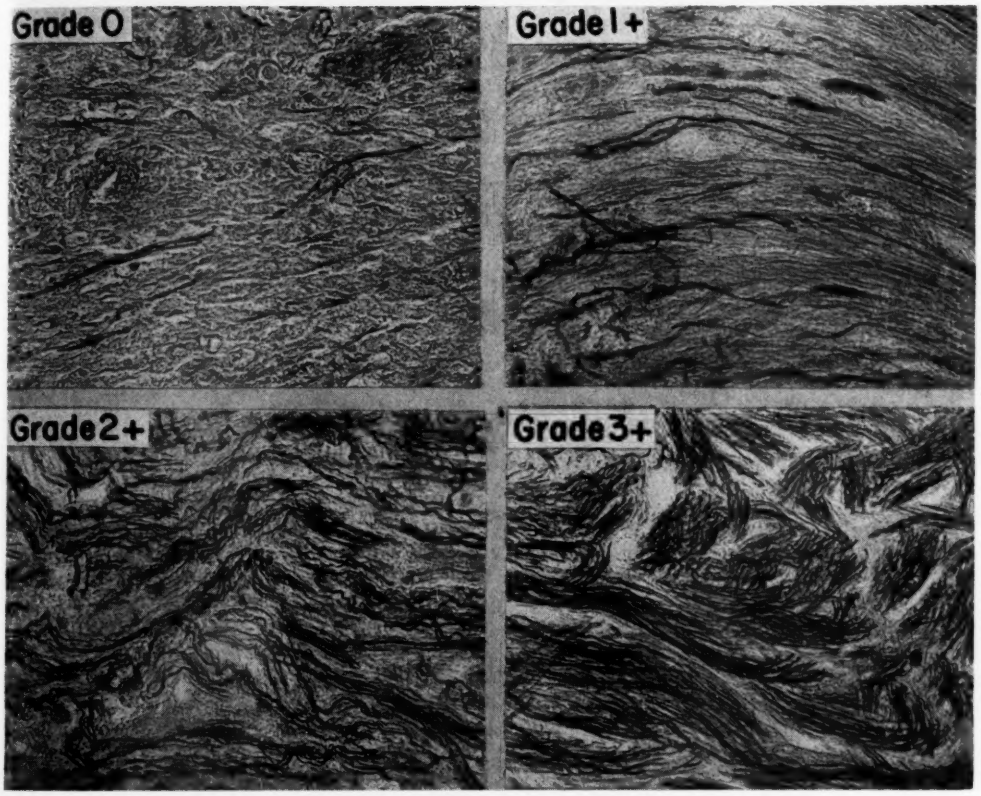



Fig. 1.—Photomicrographs of the four grades of nerve regeneration used in the evaluation of this material. Grade 0, almost complete absence of nerve regeneration as evidenced by practically no nerve fibers in scar; Grade 1 plus, few nerve fibers with minimal crossing of fibers; Grade 2 plus, moderate number of nerve fibers, more marked evidence of inter-crossing; Grade 3 plus, large number of nerve fibers, marked intercrossing. × 283.

left nerve was treated by one of the following methods:

*Group* 1: The nerve was ligated with plain cotton, and the stump was cauterized with crystalline silver nitrate proximal to the ligature.

*Group* 2: The nerve was ligated with plain cotton, and the stump was injected with 0.1 cc. of 50 per cent aqueous solution of procaine hydrochloride proximal to the ligature.

*Group* 3: The nerve was ligated with plain cotton, and the stump was injected with 0.1 cc. of 1 per cent maleic hydrazide solution proximal to the ligature.

*Group* 4: The nerve was ligated with plain cotton and injected with 0.1 cc. of undiluted undecylenic acid proximal to the ligature.

*Group* 5: The nerve was ligated with cotton thread impregnated with radioactive chromic phosphate with an assay value ranging from 0.4 to 5.6 microcuries per centimeter of ligature material in the various groups of animals treated by this method.

The substances used in Groups 1 to 4 were ordinary stock material. Silver nitrate was selected as a typical caustic agent. Procaine hydrochloride solution was used to determine its effect when injected intraneurally in high concentration. Maleic hydrazide solution, known to have growth-arresting effects on certain plants, was tested as a water-soluble growth inhibitor. Undecylenic acid is a widely used fungistatic agent. Because it is insoluble in water, it was hoped that it would remain at the site of its intraneural injection for a prolonged period, thus exerting a sustained effect on the cellular elements of the nerve stump.

The radioactive chromic phosphate was secured from Abbott Laboratories in colloidal suspension. In preparing chromic radiophosphate, the initial precipitate is thoroughly washed, fused at high temperature to render it insoluble and milled to required particle size to produce colloid (Abbott Laboratories). The $P_{32}$ in the material has a half life of fourteen and three-tenths days, emits beta particles with a maximum energy of 1.7 MEV and has an effective ionizing radiation range of 2 to 7 mm. in tissues. If strictly local effect is desired, the $CrP_{32}O_4$ should b prepared in particle sizes ranging betwee 2 and 4 microns. With these particle sizes approximately 85 per cent of the inter stitially deposited isotope remains at th site of application.[5] One microcurie o $CrP_{32}O_4$, when completely disintegrating delivers a total dose of 885 REP to the surrounding 1 gram or 1 cubic centimeter of tissue, each beta particle producing 8 ion-pairs per millimeter of tissue and thus yielding a high linear density ionization.

The radioactive chromic phosphate was incorporated into cotton thread by placing the latter into the frequently agitated isotope suspension until the filaments became saturated, after which the material was dried and the cotton thread assayed for its isotope content per centimeter. Since the colloidal chromic phosphate immediately becomes firmly anchored to the cotton, there was good control over the dosage, which was measured in terms of the length of thread. As a rule, after the ligature was tied, one end of the knot was cut short, while the other end was left 0.5 to 0.75 centimeter long and was placed parallel to the nerve in order to insure ir-

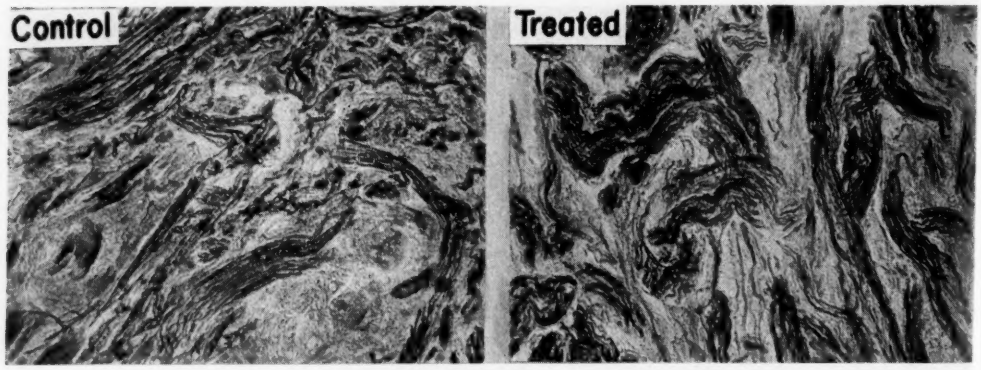



Fig. 2.—Representative regions of control and maleic hydrazide-treated sciatic nerve stumps showing nerve fiber infiltration and connective tissue changes in the control sciatic nerve stump and in the contralateral treated sciatic nerve end. In this typical case, the fields selected for this illustration lay rostral to the ligatures in portions of the amputation neuromas which developed in the peripheral scars. Both specimens graded 3 plus. Rat No. 173, × 283.

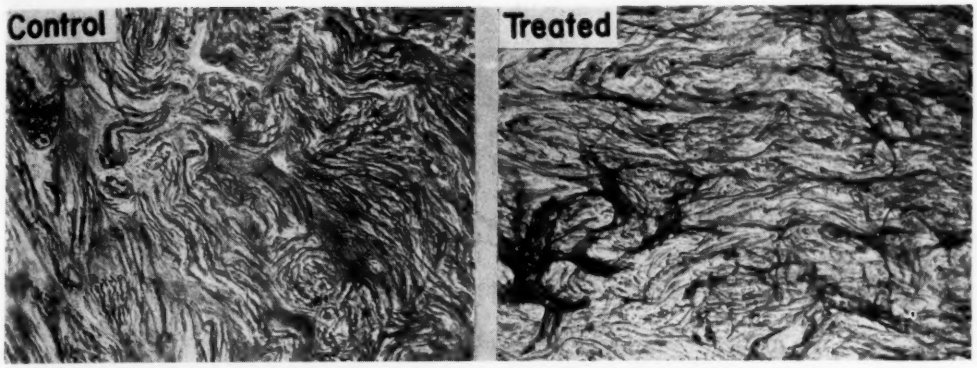



Fig. 3.—A typical example of changes observed in control and silver nitrate-cauterized sciatic nerve ends. An example of the lesser degree of nerve regeneration after application of silver nitrate in 1 of 2 animals. The silver nitrate-treated sciatic stump displays some of the artifacts commonly seen after its application. The cauterized specimen contains fewer new nerve fibers than does the control nerve stump. In addition, these nerve elements display less interlacing and interweaving. Control graded 3 plus; treated graded 2 plus. Rat No. 177, × 283.

radiation of the terminal segment of the stump.

This technic prevented accidental contamination of the wound, a danger inherent if the material is injected, especially if the structure is as small as the sciatic nerve of the rat. Furthermore, the larger particles of the chromic phosphate have a tendency to precipitate and to adhere to the glass, especially if the syringe is not agitated during the injection.

The animals were killed ninety to four hundred and forty days after the operation. Two-centimeter segments of the proximal control (right) and the treated (left) nerve stumps were removed, fixed in ammonia alcohol and stained by the pyridine method of Ranson, as described by Conn and Darrow,[6] and sectioned serially.

*Clinical Experiments.* — Radioactive chromic phosphate was employed for neuroma prophylaxis in 16 human patients. In this clinical series the $CrP_{32}O_4$ was injected either with a small-gauge needle proximal to the ligature of the nerve stump or via a fine polyethylene catheter advanced 5 to 14 cm. into the nerve trunk. The isotope suspension was deposited while the tube was slowly withdrawn.

*Results.*—An arbitrary scale was established to permit evaluation and comparison of the histologic changes in the control and treated sciatic nerve stumps. Grading was based on the relative density of regenerated nerve fibers, together with the degree of aberrant growth patterns exhibited by the nerve sprouts. Grade 0 indicated almost complete absence of nerve regeneration in the proximal stump. Grade 1 indicated the presence of a few new elements in the scar and minimal crossing of the fibers. Greater densities of nerve sprouts with correspondingly more pronounced aberrant crossing of the filaments were graded 2 or 3, depending on the presence of lesser or greater degrees of disorganization. Each of the four grades is illustrated in Figure 1.

Since evidence of suppression of nerve regeneration was derived from a comparison of the treated sciatic nerve stump and the control (untreated) contralateral sciatic stump of the same animal, each animal was its own control. Observations made in those instances in which only one

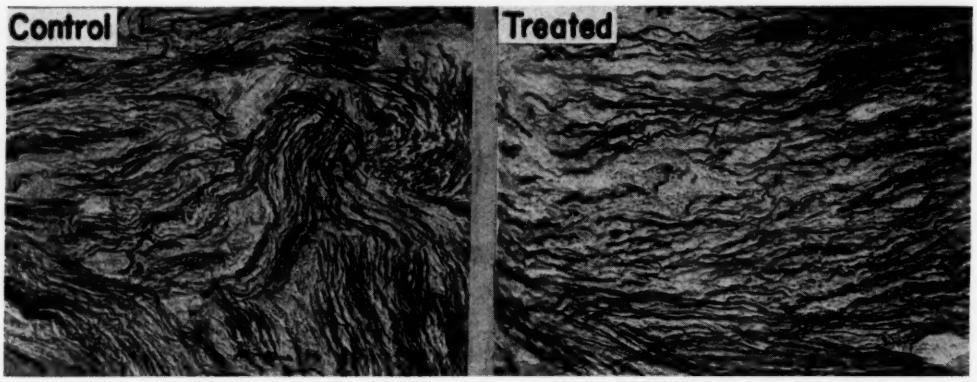



Fig. 4.—Representative example of control and 50 per cent procaine hydrochloride-treated sciatic nerve stumps in which neuroma formation was inhibited by the procaine. Note the greater disorganization of fibers in the control as compared to the treated nerve. Control specimen graded 3 plus; treated specimen, 1 to 2 plus. Rat No. 168, × 283.

nerve was available for study are not included in this report.

*One Per Cent Maleic Hydrazide Solution*: This agent has been demonstrated to inhibit growth of certain plants.[7] It was injected into the left sciatic nerve stump in a series of 12 rats.

Microscopically, both the control and the treated sciatic nerve stumps of 10 animals displayed marked evidence of regeneration. In 4 of these the intensity of the nerve influx, as measured by the density of new nerve fibers and the degree of interlacing displayed by these elements, was greater in the treated sciatic nerves than in their corresponding controls. A marked proliferation of connective tissue was apparent in all of the treated stumps (Fig. 2).

The sciatic nerves of two of the 12 animals treated with maleic hydrazide showed somewhat fewer new nerve elements than did their controls; the nerve sprouts were sufficiently numerous, however, to suggest that maleic hydrazide had little effect upon the regeneration of nerve elements.

*Silver Nitrate*: A crystal of silver nitrate was applied to the ligated proximal stump of the left sciatic nerve in a series of rats. The evaluation of nerves subjected to this compound has been, in our experience, relatively difficult as compared to the specimens treated with other substances. The deposition of numerous silver particles in the histologic preparations, together with the relative refractoriness of the silver nitrate-cauterized nerve stump to silver staining, tended, in some specimens, to obscure the tissue changes. In the 7 animals here described, however, the patterns were sufficiently clear to warrant consideration.

Five of these rats showed a similar density of nerve regeneration in the treated and in the control sciatic stumps. The stumps treated with silver nitrate from 2 animals displayed a quantitatively lesser degree of nerve regeneration and scar formation than did the untreated nerve (Fig. 3).

The observations in this series of animals indicate that silver nitrate is relatively ineffective in the prevention of amputation neuromas, as judged by the standards used to evaluate nerve regeneration in our studies.

*Fifty Per Cent Procaine Hydrochloride*: The effect of 50 per cent procaine hydro-

chloride upon the formation of amputation neuromas was studied in 8 rats. Comparison of the control and treated sciatic nerve stumps in half of these animals failed to reveal significant evidence of inhibition of nerve regeneration, since an equal influx of nerve elements was observed in the treated and the control stumps. Moreover, the same degree of crisscrossing and interweaving of new nerve sprouts was present in the sciatic stumps treated with 50 per cent procaine hydrochloride as in the contralateral controls.

The other 4 animals in this series displayed evidence of impeded nerve fiber infiltration into the treated nerve ends, in that fewer new nerve elements were present in the procaine-infiltrated sciatic stump, with less evidence of interlacing of these nerve elements than was observed in the controls (Fig. 4).

On the basis of the observations made on these 8 animals it was concluded that 50 per cent procaine hydrochloride may have limited value in the treatment of amputation neuromas.

*Undecylenic Acid*: One-tenth centimeter of undiluted undecylenic acid was injected into the proximal stump of the left sciatic nerve of 16 animals. Subsequent examination of the nerve stumps revealed that 9 of this group of rats displayed fewer new nerve fibers in the treated than in the control nerves, though the difference was not as marked as that observed in certain other series in which other forms of treatment were employed. In 6 of the 9 animals a substantial number of nerve fibers penetrated the stump of the treated specimen. Although this influx was less than that observed in the control specimen in each case, there was enough nerve regeneration in the sciatic nerve stumps treated by injection of undecylenic acid to suggest that this substance had not been strikingly effective in inhibiting the growth of new nerve elements (Fig. 5).

In all of the remaining animals in the undecylenic acid series, symmetric neuromas developed. Neither evidence of differential density nor a decrease of the interlacing characteristic of the invading elements was observed. In fact, in 3 of the rats the treated nerve stumps displayed even greater density of regenerated nerve fibers than did the control nerves.

While 9 of the 16 animals gave some evidence of suppression of regeneration in the treated stumps as compared with their controls, 7 failed to give any in-

Fig. 5.—Example of undecylenic acid-treated sciatic nerve stumps and corresponding control nerve. Control graded 3 plus; treated nerve graded 2 plus. Rat No. 110, × 283.

dication that growth had been inhibited. The results in this series of animals suggest that undecylenic acid is relatively ineffective in the prevention of amputation neuromas.

*Radioactive Chromic Phosphate:* The effect of beta radiation, emitted by radioactive chromic phosphate, upon nerve regeneration was studied in 48 animals. They were killed ninety to four hundred and forty days after division of the sciatic nerves and unilateral placement of the $CrP_{32}O_4$ impregnated ligature.

Forty-three of the 48 nerve stumps treated with $CrP_{32}O_4$ displayed a moderate to marked decrease in the density of new nerve fibers as compared to the untreated control. This decrease was paralleled by a decrease in the amount of interlacing and interweaving of what few neural elements did enter the scar (Fig. 6 *A* and *B*).

Comparison of the control and irradiated nerve stumps indicated that regeneration had been suppressed to varying degrees in approximately 88 per cent of these animals. In an attempt to determine whether this varying influx was related to the amount of radiation delivered to the stump, we have divided the animals treated with chromic phosphate into three groups, according to the isotope content of the impregnated cotton thread used for ligation of the left sciatic nerve. Although the assay of the radioactivity per unit length of ligature material allows only approximations of the actual amount of radiation delivered to the nerve stump target, correlations were observed in these studies. Our figures suggest that higher radiation dosage is a determining factor in inhibiting nerve regeneration. For example, ligatures containing 0.4 to 0.7 microcuries per centimeter suppressed the ingrowth of nerve sprouts in 6 of the 8 animals examined. With 1.3 to 2.37 microcuries per centimeter of ligature, 19 of 21 animals gave evidence of inhibited nerve growth. Ties containing 3.65 to 5.6 microcuries per centimeter prevented neuromas in 18 of 19 rats. Suppression of the growth of nerve elements into the scar was evident even eighteen months after treatment of the stumps.

These observations indicate that locally applied radioactive colloidal chromic phosphate is decidedly effective in preventing or reducing neural regeneration in the treated nerve stumps.

The results of this study are summarized in Figure 7. Here the incidence of bilaterally symmetric neuroma formation and the incidence of suppression of nerve regeneration in the treated nerves as compared to their controls are plotted in percentages. Although the number of animals in a few groups is too small to be significant, the chart provides an opportunity for comparison of the influence of the various agents employed.

It is evident from this chart that the application of maleic hydrazide or silver nitrate has, by our criteria, little effect upon the regeneration of nerve fibers. Somewhat more favorable though unimpressive results were obtained with both undecylenic acid and 50 per cent aqueous procaine hydrochloride. The single agent in our series that appeared to be consistently effective in significant suppression of nerve sprout influx into the sciatic nerve stumps was radioactive chromic phosphate.

*Results of Clinical Study.*—No painful syndrome was reported by the patients in a small clinical series of nerve stumps treated with radioactive chromic phosphate.

Two nerve stumps so treated were secured at autopsy. The patient in Case 14 (see table) survived only fourteen days after amputation and will be described in a later report. The other treated sciatic nerve is from the patient in Case 2, a 76-year-old diabetic women who died three

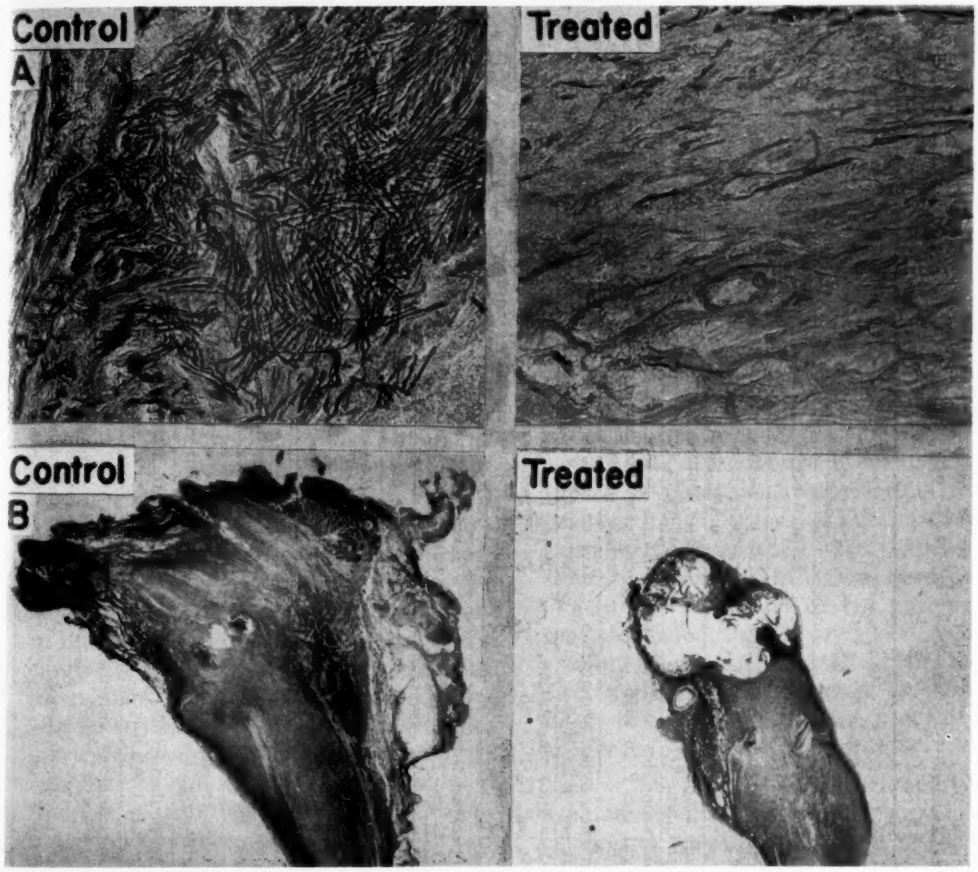



Fig. 6.—Photomicrographs of the control and the radioactive chromic phosphate-treated sciatic nerve stumps. *A*, control stump shows marked evidence of regeneration. Nerve stump treated with radioactive chromic phosphate shows little if any evidence of invasion by new nerve elements. Control graded 3 plus; treated nerve graded 0. Rat No. 220, × 283. *B*, changes observed in control and treated specimens with low power magnification (× 16). Rat No. 123.

hundred and eighty-four days after supracondylar amputation of the left thigh. The distal 14 cm. of this nerve was injected with 125 microcuries of radioactive chromic phosphate, which was deposited within the nerve with a polyethylene catheter after the nerve was divided in the course of the amputation.

Sections of the terminal 5 cm. of this nerve show pronounced reduction of fibroblastic and axonal elements in the central tract, which was the site in which the $CrP_{32}O_4$ had been deposited, as compared to the periphery of the nerve trunk, which, being more distant from the isotope deposit, received less radiation. Grossly, this nerve stump had no terminal bulb.

A short documentation of these cases is presented in the accompanying table.

## COMMENT

The objective of neuroma prophylaxis is the inhibition of growth. Peripheral

*Summary of Clinical Cases with $CrP_{32}O_4$ Therapy*

| *Patient and Sex Case No. of Patient* | *Age* | *Diagnosis* | *Operation* | *Microcuries of Radioactive Chromic Phosphate Injected into the Nerve* | *Postoperative Incidence of Pain Phantom* |
|---|---|---|---|---|---|
| 1 M | 61 | Diabetes; gangrene, right leg | Supracondylar amputation, right leg, 9/5/1953 | 50 μc. isotope into sciatic stump | None |
| 2 F | 76 | Diabetes; gangrene, left foot | Supracondylar amputation, left leg, 11/13/1954 | 125 μc. isotope via polyethylene catheter into proximal 14 cm. of sciatic stump | None |
| 3 F | 14 | Osteogenic sarcoma | High amputation, left thigh, 6/14/1955 | 100 μc. isotope 2 cm. proximal to ligature of sciatic stump | None |
| 4 F | 51 | Arteriosclerotic gangrene, right foot | Supracondylar amputation, right leg, 8/16/1955 | 115 μc. isotope via polyethylene catheter into proximal 12 cm. of sciatic nerve | None |
| 5 F | 77 | Diabetes; gangrene, left foot | Supracondylar amputation, left leg, 4/28/1955 | 150 μc. isotope via catheter into proximal 10 cm. of sciatic nerve | None |
| 6 M | 60 | Diabetes; gangrene, left foot | Below knee amputation, left leg, 12/10/1955 | 37 μc. into posterior tibial nerve; 25 μc. into peroneal nerve | None |
| 7 M | 56 | Arteriosclerosis; gangrene, left foot | Supracondylar amputation, left leg, 12/31/1955 | 150 μc. isotope via catheter into proximal 12 cm. of sciatic nerve | None |
| 8 M | 64 | Arteriosclerosis; gangrene, left foot | High amputation, left thigh, 1/16/1956 | 75 μc. isotope into proximal sciatic stump, 2 cm. above ligature | None |
| 9 F | 73 | Diabetes; gangrene, right foot | Supracondylar amputation, right leg, 9/18/1956 | 145 μc. isotope 1-2 cm. proximal to ligature of sciatic stump | None |
| 10 F | 73 | Diabetes; gangrene, left foot | Supracondylar amputation, left leg, 11/28/1956 | 40 μc. isotope into sciatic stump | Died 6th postoperative day |
| 11 F | 71 | Carcinoma, left lung | Left pneumonectomy, 5/15/1956 | 25 μc. isotope into stump of 4th intercostal nerve | Not evaluated for phantom syndrome |
| 12 F | 78 | Arteriosclerosis; gangrene, right foot | Supracondylar amputation, right leg, 9/21/1956 | 50 μc. isotope above ligature of sciatic stump | None |
| 13 F | 65 | Carcinoma, right lung | Wedge resection of right lung, 10/11/1956 | 15 μc. isotope into 4th intercostal nerve | Not evaluated for phantom syndrome |
| 14 F | 73 | Osteomyelitis of right 5th toe | Exarticulation of right 5th toe, 1/3/1957 | 15 μc. into fifth plantar and dorsal digital nerves | None |
| 15 F | 57 | Diabetes; gangrene, right foot | Supracondylar amputation, right leg, 4/8/1957 | 250 μc. into proximal 5 cm. of sciatic stump | None |
| 16 F | 63 | Bronchogenic carcinoma, left lung | Left pneumonectomy, 4/9/1957 | 50 μc. isotope into stump of 3d intercostal nerve | Not evaluated for phantom syndrome |

nerves regenerate through the combined activity of at least three types of cells: fibroblasts of the endoneurium, Schwann cells and the neuron.[8]

Although fibroblasts do not follow a definite pattern of proliferation, the Schwann cells grow as a more or less cylindric tuft along which, or into which, the nerve sprouts advance from the central stump.[9]

The most important elements in the regeneration of the nerve fibers are the neurons. Greatly elongated processes extend from the central cell bodies to form peripheral nerves. Although adult neurons cannot multiply, their intact cell bodies do exhibit remarkable growth energy in the process of regenerating their amputated axons or dendrites, For example, during regeneration, axoplasm is formed at such a rate that the cell body must build several times its volume per day.[10] This neuroplasm is manufactured in the perikaryon of the cell body[3] and is carried to the periphery by an "axomotile" mechanism (as postulated by Weiss and Hiskoe[11]). This continuous, centrifugally advancing neuroplasm forms terminal accumulations if its progress is blocked. Thus, the distal segment of the regenerating nerve fiber may become telescoped, coiled, beaded or ballooned when it encounters an obstruction.[12] Since certain neurons appear to maintain the ability to produce fresh neuroplasm for years after their peripheral processes have been sectioned, it is not suprising that the deformities of nerve sprouts invading the scar of the proximal stump of an amputated nerve may be accentuated with time.[11]

The various procedures that have been suggested or tried for the prevention of nerve regeneration must be evaluated in the light of the aforedescribed mechanism. Neither nerve stump ligation, plastic operation on the stump, implantation of the stump into muscle, bone, or the nerve itself prevents proliferation of fibroblasts and Schwann cells or the piling up of the blocked axoplasm above the site of the mechanical obstruction. Furthermore, it would appear that after the application of necrotizing chemicals or a thermal injury to the nerve stump (alcohol, phenol, formaldehyde, cautery, freezing, electrodesiccation), in addition to the various types of mechanical obstruction, the applied agent and the necrotic débris would be absorbed, and the unceasing growth of the cellular elements would result in neuroma.

This is in agreement not only with the observations of Pinto and Junqueira,[4] but with the results of the present study, in which neuromas developed in 50 to 83 per cent of rats after the use of silver nitrate, saturated procaine hydrochloride and 1 per cent maleic hydrazide solutions. These experiments reflect the effect of a single *unsustained* chemical insult applied to the ligated central stump of the nerve. On the other hand, local application of radioactive chromic phosphate, which represents a *prolonged or sustained* biochemical insult to the growing tissue, proved to be an effective neuroma inhibitor.

In spite of the present inability to evaluate precisely the radiation-induced changes in the component parts of the cell, clinical, experimental and histopathologic observations permit certain conclusions to be drawn with regard to the influence of radioactive chromic phosphate upon the connective tissue elements and sheath cells involved in nerve regeneration. For example, there is ample evidence that young cells are more susceptible to injury from irradiation than are mature cells.[13] Cells in the process of division, particularly in certain phases of mitosis, are especially vulnerable to ionizing irradiation,[14] and proliferation of fibroblasts are inhibited by ionizing irradiation.[15] Furthermore, successful prophylaxis and treatment of keloids by means of ionizing irradiation[16] leaves no doubt about the effectiveness of

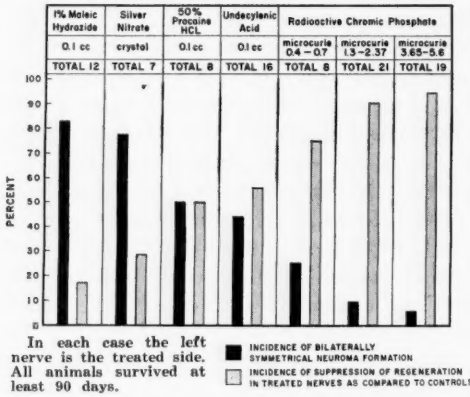



Fig. 7.—Chart indicating results of various methods employed in this series.

this modality in the suppression of fibroplasia. Arrest of the intense multiplication of the fibroplasts during nerve regeneration, therefore, can reasonably be expected when the growing tissue is exposed to prolonged ionizing irradiation.

Moreover, fibroblastic activity is inhibited far beyond the period of actual irradiation, the prolonged effect of beta rays upon connective tissues having been reported to last for three months to two years after exposure.[17]

The nerve stumps in this series which were treated with radioactive chromic phosphate and exhibited little or no evidence of nerve regeneration displayed a concomitant decrease or absence of new fibroblastic elements. Furthermore, the treated nerves in which some nerve sprouts had succeeded in invading the scar, even though in greatly reduced numbers as compared to the corresponding control specimen, always displayed substantial fibroblastic proliferation at the site of surgical division of the nerve.

There is little information with regard to the sensitivity of Schwann cells to radiation. Schwann cells are of epithelial origin. They exhibit intense growth activity after section of the nerve, and during this period of frequent cell division it is possible that they are vulnerable to radiation injury. Since Schwann cells make the most important contribution to the normal metabolism of the axons,[18] they are essential to the functional integrity of the latter; therefore, sustained radiation interference with the posttraumatic proliferation of the Schwann cells would be expected to affect the growth of the axis cylinder.

Though inhibition of nerve regeneration by $CrP_{32}O_4$ is demonstrable, we are unable to state whether the inhibited axonal growth is an indirect result of the suppression of growth of the Schwann cells or the fibroblasts, or is the direct result of the ionizing irradiation of the neuroplasm itself. Under optimal circumstances the axoplasm of the divided neurons sprouts about 2 mm. per day.[11] If this advance is slowed down by mechanical constriction (ligature) of the neurolemmal tubes, and the blocked axonal stumps are then exposed to a sustained crossfire of high linear density ionizing irradiation, it might be assumed that first their enzyme regulatory mechanism and later the enzymes themselves may be affected. The result might be loss of the essential enzyme systems of the peripheral axoplasm. The high degree of sensitivity of sulfhydril metabolism to radiation is a possible clue to certain phases of the events that transpire when a living cell, or part of one, e.g., the axis cylinder of a neuron, is exposed to beta rays.[19]

## SUMMARY

1. Controlled experimental studies were made on rats by applying 1 per cent maleic hydrazide solution, 50 per cent aqueous procaine hydrochloride solution, silver nitrate crystal, undecylenic acid, and radioactive colloidal chromic phosphate to the ligated central stump of the sciatic nerve.

2. The application of maleic hydrazide solution, undecylenic acid, silver nitrate and 50 per cent procaine hydrochloride solution was observed to be relatively ineffective in the prevention of neuromas.

3. The use of radioactive chromic phosphate-impregnated ligature on the central stump of the sciatic nerve of the rat inhibited nerve sprout regeneration in 88 per cent of the treated stumps as compared with the contralateral stump in the same animal.

4. Higher isotope content of the impregnated ligature material yielded a greater degree of growth inhibition in the treated nerve stumps.

5. Injection of 25 to 250 microcuries of radioactive colloidal chromic phosphate into the central stumps of resected or amputated nerves was made in 16 clinical cases. Painful phantom syndrome did not develop in this small series of patients.

**Acknowledgments:** We wish to express our appreciation to Doctors T. E. Baffes, J. H. Brown, K. Eggen, J. D. Guerra, T. D. Hall, G. W. Holmes, T. J. Mudge, C. A. Norberg and N. M. Percy for their cooperation in the use of chromic radiophosphate on their clinical cases, to Dr. Frederick Feiler for his valuable assistance during a period of this study and to Dr. George Milles for reviewing the manuscript.

RÉSUMÉ

1. Des études expérimentales contrôlées ont été faites chez le rat par l'application sur le moignon central ligaturé du nerf sciatique, d'une solution à 1% d'hydrazide maléique, d'une solution aqueuse de chlorhydrate de procaïne à 50%, de nitrate d'argent cristallisé, d'acide undécylinique et de phosphate de chrome colloïdal radioactif.

2. Cette application s'est révélée pratiquement sans effect dans la prévention des neuromes.

3. L'utilisation d'une ligature imprégnée de phosphate de chrome radioactif sur le moignon central du nerf sciatique inhibé a provoqué chez le rat une régénérescence dans 88% des moignons traités, par rapport au moignon du côté opposé chez le même animal.

4. Une ligature imprégnée d'un pourcentage plus élevé d'isotopes a donné lieu à une inhibition de croissance plus forte des moignons traités.

5. Une injection de 25 à 250 microcuries de phosphate de chrome colloïdal radioactif dans le moignon central de nerfs réséqués ou amputés, a été faite dans 16 cas cliniques. Aucun syndrome douloureux ne s'est développé dans ce petit nombre de cas.

SUMARIO

1. Estudos experimentais foram feitos em ratos aplicando uma solução de hidrazida maleica a 1%, 50% de cloridrato de procaina, cristais de nitrato de prata, acido undecilenico e fosfato crômico coloidal radioativo no côto central ligado do nervo ciático.

2. A aplicação de solução de hidrazida maleica, acido undecilenico, nitrato de prata e solução de cloridato de procaina a 50% mostrou-se pouco efetiva na prevenção dos neuromas.

3. O uso de fosfato cromico radioativo impregnando o coto do nervo ligado inibiu a regeneração em 88% dos cotos tratados em comparação com o coto controlateral do mesmo rato.

4. O conteudo elevado de radioisotopo no material de ligadura reduzio grandemente o crescimento nos nervos assim tratados.

5. A injeção de 25 a 250 microcuries de fosfato cromico radioativo nos cotos centrais de nervos resecados ou amputados foi feita em 16 casos clínicos. A sindrome dolorosa do membro fantasma não se estabeleceu nessa pequena serie de pacientes.

ZUSAMMENFASSUNG

1. Es wurden mit Kontrollversuchen einhergehende Untersuchungen an Ratten vorgenommen, bie denen in den abgebundenen zentralen Stumpf des Ischiasnerven

eine einprozentige maleinsaure Acrylhydrazinlösung, eine fünfzigprozentige Novocainlösung, Silbernitratkristalle, Undecylensäure und radioaktives kolloidales Chromphosphat eingeführt wurden.

2. Die Anwendung der maleinsauren Acrylhydrazinlösung, des Silbernitrats und der fünfzigprozentigen Novocainlösung erwies sich als verhältnismässig wirkungslos zur Verhütung der Entwicklung eines Neuroms.

3. Die Verwendung einer mit radioaktivem Chromphosphat imprägnierten Ligatur am zentralen Stumpf des Ischiasnerven der Ratte verhinderte eine spriessende Regeneration des Nerven in 88% der so behandelten Stümpfe verglichen mit dem Kontrollstumpf auf der anderen Seite desselben Versuchstieres.

4. Ein höherer Isotopengehalt des Materials, mit dem die Ligatur imprägniert war, ergab einen höheren Grad der Wachstumsbehinderung in den behandelten Nervenstümpfen.

5. In 16 klinischen Fällen wurden in den zentralen Stumpf resezierter oder amputierter Nerven 25 bis 250 Microcuries radioaktiven kolloidalen Chromphosphats eingespritzt. In dieser kleinen Gruppe von Kranken kam es nicht zur Entwicklung eines schmerzhaften Phantomsyndroms.


RIASSUNTO

1. E' stata fatta una ricerca sperimentale sul ratto consistente nell'applicazione di soluzioni di idrazide all'1%, di novocaina al 50%, di nitrato d'argento, di acido undecilenico e di fosfato cromico colloidale radioattivo sul capo prossimale di sezione dello sciatico.

2. Si è visto che l'applicazione dell'idrazide, dell'ac. undecilenico, del nitrato d'argento e della novocaina è pressochè inefficace nella prevenzione dei neuromi.

3. L'impiego del fosfato di cromo radioattivo, invece, impedisce la rigenerazione nell'88% dei casi.

4. Quanto maggiore è il contenuto di isotopi tanto maggiore è l'effetto inibente sulla crescita del moncone nervoso.

5. In 16 casi clinici venne fatta l'iniezione di 25-250 microcuries di fosfato cromico colloidale radioattivo nel capo centrale di trochi nervosi amputati e in nessuno di essi si ebbe la comparsa della sindrome dolorosa da amputazione.


REFERENCES


1. Mountcastle, V., and Henneman, E.: Pattern of Tactile Representation in Thalamus of Cat, J. Neurophysiol. 12:85, 1949. Woolsey, C. N.: Patterns of Sensory Representation in the Cerebral Cortex, Fed. Proc. 6:437, 1947.

2. Eccles, J. C.: Neurophysiological Basis of the Mind. London: Oxford University Press, 1953. Lloyd, D. P. C.: Post-tetanic Potentiation of Response in Monosynaptic Reflex, J. Gen. Phys. 33:147, 1949.

3. Bardenhauer: Behandlung der Nerven bei Amputationen zur Verhuetung der Amputationsneuromen und zur Heilung der bestehenden Neurome durch die sogenannt Neurinkampsis, Deutsche Ztschr. f. Chir. 96:126, 1908. Bate, J. I.: Method for Treating Nerve Ends in Amputation Surgery, Am. J. Surg. 64:373, 1944. Beswerschenko, A. P.: Traumatische Neuroma: Entstehungsbedingungen der Neurome und Mittel zur ihrer Verhuetung: Experimentelle Untersuchungen, Zntrlbl. f. Chir. 56:455, 1929. Boldrey, E.: Amputation Neuroma in Nerves Implanted in Bone, Ann. Surg., 118:1052, 1943. Chapple, W. A.: Reamputation, Brit. M. L., 2:242, 1917. Chenilleau, P.: Recherches experimentales sur les ligatures des nerfs, Bordeau chir. 69, 1947. (Cited by Pinto, V. A. de C., and Junqueira, L. C. U.: Comparative Study of Methods for Prevention of Amputation Neuroma, Surg., Gynec. and Obst. 99:492, 1954.) Cieslak, A. K., and Stout, A. P.: Traumatic and Amputation Neuromas, Arch. Surg. 53:646, 1946. Corner, E. M.: The Structure, Forms and Conditions of the Ends of Divided Nerves; with a Note on Regeneration Neuromata, Brit. J. Surg. 6:273, 1918. Dogliotti, A. M.; Teneff, S., and Micheli, E.: Amputazioni e disarticolasioni. In Dogliotti, A. M.; Tecnica Operativa. Torino: Edit. Torinese, 1948, vol. 1. Edds, M. V., Jr.: Prevention of Nerve Regeneration and Neuroma Formation by Caps of Synthetic Resin, J. Neurosurg. 2:507, 1945. Foerster, O.: Die Leitungsbahnen des Schmerzgefühls und die Chirurgische Behandlung der Schmerzzustände. Berlin and Vienna: Urban und Schwarzenberg, 1927. Guttmann, L., and Medawar, P. B.: The Chemical Inhibition of Fiber Regeneration and Neuroma Formation in Peripheral Nerves, J. Neurol. and Psychiat. 5:130, 1942. Hedri, A.: Zur Behandlung des Nervenquerschnittes bei Amputationsstuempfen, Munch. med. Wchnschr. 67:1148, 1920.

Hedri, A.: Ein einfaches Verfahren zur Verhuetung der Trennungsneurome, Arch. klin. Chir. 117:842, 1921. Herrmann, L. G., and Gibbs, E. W.: Phantom Limb Pain; Its Relation to the Treatment of Large Nerves at Time of Amputation, Am. J. Surg. 67:168, 1945. Huber, G. C., and Lewis, D.: Amputation Neuromas; Their Development and Prevention, Arch. Surg. 1:85, 1920. Hyden, H.: Die Function des Kernkörperchens bei der Eiweissbildung in Nervenzellen, Ztschr. f. Mikr. Anat. Forsch. 54:96, 1943. Kruger, von: Ueber Nervenquetschung Zur Verhuetung schmerzhafter Neuroma nach Amputationen, Much. med. Wschr. 1:368, 1916, (Cited by Pinto, V. A. de C., and Junqueira, L. C. U.: Comparative Study of Methods for Prevention of Amputation Neuroma, Surg., Gynec. and Obst. 99:492, 1954.) Laewen, A.: Die Anwendung der Nervendurchfrierung nach W. Trendelenburg bei Amputationen und der Operation Traumatischer Neurome, Zntrlbl. f. Chir. 32:626, 1919. Laewen, A.: Ueber Nervenvereisung bei Amputationen, Amputationsneuromen, Angiospasmen, Erythromelalgie, seniler Gangraen und Ulcus cruris varicosum, Beitr. klin. Chir. 133:405, 1925. Lewis, W. H.: Axon Growth and Regeneration, Anat. Rec. 91:25, 1945 (Suppl.) Lexer, E.: Chirurgische Therapie bei Erkrankungen und Verletzungen des Nervensystems. In Bumke, and Foester, Handb. d. Neurol. Berlin: 1936. Moszkowicz, L.: Zur Behandlung der schmerzhaften Neurome, Zntrlbl. f. Chir. 45:547, 1918. Padovani, P.: Les douleurs des amputes, Sem. Hop. Paris, 25:817, 1949. Padovani, P., and Mansuy, L.: Les moignons douloureaux des membres, J. Chir. Paris 63:527, 1947. Poth, E. J., and Bravo-Fernandez, E.: Prevention of Neuroma Formation by Encasement of the Severed Nerve End in Rigid Tubes, Proc. Soc. Exp. Biol. 56:7, 1944. Poth, E. J.; Bravo-Fernandez, E., and Drager, G. A.: Prevention of Formation of End-Bulb Neuromata, Proc. Soc. Exp. Biol. 60:200, 1945. Sicard, J. A.: Traitment des nevrites douloureuses de guerre par l'alcoolization nerveuse locale. Presse. Med. 24:241, 1916. Stookey, B.: Surgical and Mechanical Treatment of Peripheral Nerves. Philadelphia: The W. B. Saunders Company, 1922. Strahberger, E.: Ueber Amputationsneurome, Wien. klin. Wchnschr. 63:166, 1951. Teneff, S.: Prevention of Amputation Neuroma, J. Internat. Coll. Surgeons 12:16, 1949. Tomoff, W.: Vermeidung schmerzhafter Neurombildungen bei Amputationen durch die Methode der direkten Nervenimplantation in Muskel (Nacktneurotisation). Ztschr. ges. exp. Med. 84:287, 1932. Troitskiy, V. V.: Ligature of Nerves for Prevention of Terminal Neuromas, Khirurgia 2:261, 1945.

4. Pinto, V. A. de C., and Junqueira, L. C. U.: Comparative Study of Methods for Prevention of Amputation Neuroma, Surg., Gynec. and Obst. 99:492, 1954.

5. McCormick, J. B.; Milles, G.; Jaffe, B., and Seed, L.: Tissue Distribution of Injected Radioactive Colloidal Chromic Phosphate, Arch. Path. 58:187, 1954.

6. Conn, H. J., and Darrow, M. A.: Staining Procedures Used by the Biological Stain Commission. Biotech. Public Ed. Geneva, New York, 1943.

7. Schoens, D. L., and Hoffmann, O. L.: Maleic Hydrazide, a Unique Growth Regulant, Science 109:588, 1949.

8. Cajal, S., and Ramon, Y.: Degeneration and Regeneration of the Nervous System, Translated and edited by Raoul M. May, London: Oxford University Press, 1928.

9. Bielschowsky, M.: In Bumke and Foerster's Handb. d. Neurol. I, Berlin, 1935. Boeke, J.: Ztschr. f. Mikr. Anat. Forsch. 33:233, 1935 (Cited from Cameron, G. R.: Pathology of the Cell, Oliver and Boyd, Edinburgh and London, 1952.). Speidel, C. C.: Studies of Living Nerves, J. Exper. Zool. 61:279, 1932. Williams, S. C.: Regeneration of Peripheral Nerves in Amphibia Studies with Aid of a Vital Stain, J. Exp. Zool. 57:145, 1930. Young, J. Z.: The Functional Repair of Nervous Tissue, Physiol. Rev. 22:318. 1942. Cajal[8]

10. Gerard, R. W.: Some Aspects of Neural Growth, Regeneration and Function, Chicago: The University of Chicago Press, 1950.

11. Weiss, P., and Hiscoe, H. B.: Experiments on Mechanism of Nerve Growth, J. Expl. Zool. 107:315, 1948.

12. Weiss, P.: An Introduction to Genetic Neurology. Chicago: The University of Chicago Press, 1950.

13. Lea, D. E.: Actions of Radiation on Living Cells. Boston: Cambridge University Press, 1945. Strangeways, T. S. P., and Hopwood, F. L.: The Effects of X-rays upon Mitotic Cell Division in Tissue Cultures in Vitro, Proc. Roy. Soc. 100:283, 1926.

14. Bergonie, J., and Tribondeau, L.: Fr. Acad. Sci. Paris 143:983, 1906 (cited by Cameron, G. R.: Pathology of the Cell. Edinburgh and London: Oliver and Boyd, 1952). Lasnitzki, I.: The Effect of X-rays on Cells Cultivated in Vitro; Recovery Factory, Brit. J. Radiol. 16:61, 1943.

15. (a) Lushbaugh, C. C., and Storer, J. B.: Experimental Acute Radiodermatitis Following Beta Irradiation: II. The Inhibition of Fibroplasia. Cancer 6:678, 1953. (b) Lushbaugh, C. C., and Hale, D. B.: Experimental Acute Radiodermatitis Following Beta Irradiation: IV. Changes in Respiration and Glycolysis, Cancer 6:686, 1953.

16. Low-Beer, B. V. A.: Therapeutic Use of Radio Isotopes, G. P. 10:69, 1954.

17. McDonald, J. E., and Wilder, H. C.: The Effect of Beta Radiation on Corneal Healing, Am. J. Ophth. 40:170, 1955.

18. Maximow, A. A., and Bloom, W. A.: A Textbook of Histology. Philadelphia and London: The W. B. Saunders Company, 1944.

19. Barron, E. S., and Dickman, S.: Studies on the Mechanism of Action of Ionizing Radiation: II. Inhibition of Sulfhydryl Enzymes by Alpha, Beta and Gamma rays, J. Gen. Phys. 32:595, 1949. Barron, E. S.; Dickman, S.; Muntz, J. A., and Singer, T. P.: Studies on the Mechanism of Action of Ionizing Radiation: I. Inhibition of Enzymes by X-ray, J. Gen. Phys. 32:537, 1949. Lea.[13a] Lushbaugh and Storer.[15a] Lushbaugh and Hale.[15b]

ADDITIONAL SOURCES

Cameron, G. R.: Pathology of the Cell. Edinburgh and London: Oliver and Boyd, 1952.

Kirk, N. T.: Amputations, Lewis, I. Practice of Surgery, Vol. 3. Hagerstown, Md.: Prior Co., Inc., 1951, vol. 3.

# Obstetric and Gynecologic Surgery

## The Pathologist's Approach to Preclinical Carcinoma of the Uterine Cervix, with Special Reference to Diagnosis and Management

EDWARD H. SOULE, M.D.

ROCHESTER, MINNESOTA

THE pathologist's role in the detection of preclinical carcinoma of the uterine cervix requires three avenues of endeavor. The first is the detection in smear preparations of abnormal cells from clinically benign or invisible lesions on the cervix. The second is the orientation and processing of properly obtained and adequate material for biopsy and the insuring of complete surgical removal of the grossly invisible lesion. The third is a critical and continuous evaluation of the typical cellular changes that are the basis for a fairly reproducible diagnosis of carcinoma *in situ* or of early infiltrating carcinoma of the cervix.

Cytodetection of malignant neoplasms is not a new concept but has long been a matter of dispute among pathologists. The belief that the cytologic features rather than the histologic structure are paramount in the diagnosis of a malignant lesion was expressed nearly forty years ago by Dr. William Carpenter MacCarty, who so abhorred the morbid anatomists' approach to the carcinoma problem that he earned for himself the appellation "One-cell MacCarty." Gradually investigators began to realize that carcinoma frequently manifests itself by cytologic changes in the mucous membrane of various organs before the basement membrane is violated. In 1932 Broders stressed the need for scrutiny of the characteristics of the epithelial cell and popularized this concept by a paper describing carcinoma *in situ* of the cervix, breast, skin, colon and larynx. This paper marked a revival of the phrase "carcinoma *in situ*," a term first used by Rubin in 1918, when he described malignant changes in the epithelium of the cervix.

Although the concept of carcinoma *in situ* of the vocal cords, the ducts of the breast, the skin and adenomatous polyps of the colon has been rather widely accepted, until recently the acceptance of such an entity with reference to the uterine cervix has met with varying degrees of resistance by the pathologists.

*Program of Cytodetection of Malignant Lesions of the Cervix at the Mayo Clinic.*—The first avenue of endeavor led to the institution of a program for the cytodetection of preclinical carcinoma of the cervix at the Mayo Clinic. The program was instituted in 1948, and for the first four years the smears were made at the discretion of the gynecologist. During this period the pathologists were learning the various

Read at the Twenty-Second Annual Congress of the United States and Canadian Sections, International College of Surgeons, Chicago, Sept. 8-12, 1957.

From the Section of Surgical Pathology, Mayo Clinic and Mayo Foundation, Rochester.

The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

Submitted for publication Oct. 9, 1957.

facets of carcinoma detection by smears. In 1952 the making of smears from the cervix became a routine procedure for all women seen by the gynecologist. In 1956 the program was expanded to include the routine screening of all women over the age of 25 who were examined at the clinic. As of August, 1957, the expansion of the program has been completed.

*Incidence of Detection.*—The incidence of detection of preclinical carcinoma in 66,511 initial screening smears averaged 7.8 per 1,000 women screened (Table 1). It should be emphasized that all of the women in the initial group screened had been given a clinical gynecologic diagnosis of normal cervix or some benign lesion of the cervix. Women who come to the clinic with a diagnosis of suspicious-appearing smear or the positive presence of malignant cells in the cervical smear were deleted from the initial group screened, in order to avoid an element of selectivity in the series (Table 1). In the group listed in Table 1 under "smear and biopsy," material for the two examinations was taken on the same day. The group is included in the statistics for the obvious reason that examination of the smear would have found the lesion if the biopsy had not been done.

During the nine-year period from 1948 through 1956, 417 preclinical carcinomas were detected on examination of the smear alone, and 100 preclinical carcinomas were detected in the smear-biopsy group. Use of the smear has complemented the detection program to the extent that approximately four times the number of preclinical carcinomas of which diagnosis could be expected from biopsy alone were detected during this period.

During the same interval the pathologists at the clinic examined approximately 10,000 repeat cervical smears obtained on an average of one to two years after the initial smear. The incidence of detection for the repeat smear group was 1.9 per thousand smears, which is approximately one-fourth the rate of the pickup in the initial smear group. It is my opinion that insignificant epithelial changes may well occur with the same frequency in patients who have been screened for carcinoma by examination of cervical smears as in patients who have not previously been so tested. The fact that the pickup rate in the repeat smear group has been lower seems to indicate that carcinoma *in situ* is a significant lesion. I am also convinced that, as the repeat group of smears expands and covers a significantly greater number of years, some newly developing preclinical carcinomas will be discovered.

TABLE 1.—*Cervical Smears in Preclinical Carcinoma: 1948 Through 1956*

| | | *Preclinical Carcinoma* | | | |
|---|---|---|---|---|---|
| *Period* | *Cases* | *Smear Only* | *Smear and Biopsy* | *Total* | *Rate Per 1,000* |
| 1948-1951 | 11,738 | 67 | 34 | 101 | 8.6 |
| 1952 | 8,862 | 58 | 20 | 78 | 8.8 |
| 1953 | 9,710 | 70 | 21 | 91 | 9.4 |
| 1954 | 9,595 | 57 | 11 | 68 | 7.1 |
| 1955 | 10,613 | 83 | 10 | 93 | 8.8 |
| 1956 | 15,993 | 82 | 4 | 86 | 5.4 |
| TOTAL | 66,511 | 417 | 100 | 517 | 7.8 |

Of the 517 preclinical lesions discovered, 512 were squamous cell carcinomas of the cervix, 3 were adenocarcinomas of the endocervix, and only 2 were endometrial carcinomas.

The conventional method of classifying smears is used; they are divided into five groups, varying from negative (Group 1) to "malignant cells present" (Group 5). The probably benign, suspicious and probably malignant are Groups 2, 3 and 4 respectively. Results of the initial smear by

group for the past five years are given in Table 2. During this time 54,158 smears obtained were considered "negative for carcinoma." Examination of tissue removed subsequently revealed that 13 of these smears were falsely negative. It is impossible to establish the true incidence of false negative smears, but, as might be expected, 4 of these false negative smears were observed on rechecking to contain cells marked by the technician scanners but misinterpreted by the pathologist. The remainder must be considered "smear failures."

It will be noted that subsequent examination of tissue verified the diagnosis in 99 per cent of the satisfactory Group 5 smears as productive of carcinoma. In the compilation of these percentages the smears listed in the "unexplained" column have been eliminated from the total number, since many of the patients left the clinic without biopsy or, in some instances, inadequate biopsy material was obtained. Subsequent examination of tissue from patients who had smears of Group 4, containing probably malignant cells, yielded 88 per cent positive results for carcinoma, and subsequent examination of tissue from patients who had Group 3 smears have resulted in the detection of carcinoma throughout the years in approximately 50 per cent of patients. My colleagues and I have endeavored to keep our "index of suspicion" at this level, for if the pickup rate for smears in Group 3 drops too far we are asking for too many unnecessary biopsies, and, conversely, if the pickup rate in smears of Group 3 is much above 50 per cent we may be disregarding some atypical cells and thus missing some preclinical carcinomas. Hereafter, in this paper, these and other false positive or suspected smears will be referred to as falsely suspected or false "suspicious" smears.

TABLE 2.—*Comparison of Result by Group in Initial Smears With Result of Study of Biopsy Material in Same Cases: 1952 Through 1956*

| *Initial Smears* | | *Biopsy Material* | | | |
|---|---|---|---|---|---|
| | | *Carcinoma Detected* | | | |
| *Results by Group* | *Number* | *No.* | *Per Cent* | *No Carcinoma Present** | *Diagnosis Unexplained or Unverified* |
| 5 | 189 | 178 | 99† | 2 | 9 |
| 4 | 152 | 124 | 88 | 16 | 12 |
| 3 | 254 | 112 | 51 | 104 | 38 |
| 2 | 17 | 3 | | 13 | 1 |
| 1 | 54,158 | 13 | | | |

*Thus smear diagnosis was proved to be false "suspicious."

†Percentage based on total number of initial smears minus unexplained group.

TABLE 3.—*Primary Smear Diagnosis of "Suspicious" Shown to be False by Examination of Adequate Biopsy Material: 1954 Through 1956*

| | *Smear Group* | | | |
|---|---|---|---|---|
| Result of biopsy | 2 | 3 | 4 | Total |
| Negative | 6 | 30 | 1 | 37 |
| Basal cell hyperplasia | 1 | 9 | 2 | 12 |
| Dysplasia and atypism | 1 | 37 | 6 | 44 |
| Decidual reaction, leukoplakia, or agitated cells* | | 3 | | 3 |

*One case each.

*Methods of Obtaining Material.*—The second avenue of endeavor leads to a discussion of methods for obtaining material for cytologic diagnosis.

*The Smear*: Since 1943, when Papanicolaou and Traut first won wide favor for the aspiration of the vaginal pool for exfoliative cytologic studies, no less than seven methods have been devised for the collection of cytologic material from the uterus. At the Mayo Clinic my colleagues and I have found that scraping the

portio vaginalis and endocervix with the Ayre spatula is the most satisfactory method of collecting material both from the standpoint of the clinician and from that of the pathologist. No attempt has been made to detect asymptomatic endometrial carcinomas, as the results obtainable do not seem to justify the time and expense involved. Endocervical aspiration on rare occasions, however, will lead to the detection of an endocervical carcinoma that might be missed with surface scrapings of the squamocolumnar juncture. At present we are endeavoring to evaluate this procedure; at present we have no conclusive evidence for or against its use.

The smears are fixed immediately in 95 per cent ethanol and stained with hematoxylin and eosin. The smear should be immersed immediately in the ethanol, as partial or complete drying of the preparation will distort the cells to such an extent that an inexperienced observer may interpret the nuclear artifacts as suggestive of carcinoma cells.

In our laboratory we employ seven trained technicians as scanners. They mark all smears that contain suspicious-appearing or atypical cells for special consideration by the pathologist. All unmarked smears are scanned quickly by the pathologist to evaluate the adequacy of the preparation and to spot-check the work of the technicians. Between 2.5 and 5 per cent of the total number of smears screened in this laboratory are unsatisfactory and have been deleted from the statistics here presented.

*The Biopsy*: When a cervical smear is interpreted as suspicious or positive for carcinoma, the method of obtaining adequate tissue for histologic interpretation becomes a matter of great concern to the pathologist. In a small percentage of cases, despite rather wide experience in this field by the surgeons. we are still plagued by unsatisfactory material for histologic interpretation. When a punch or conizing specimen is being obtained, the value of using compound solution of iodine (Lugol's solution) to outline the squamocolumnar juncture cannot be overstressed. Cautery should not be applied for hemostasis after punch biopsy specimens are removed, as the primary specimens fail to show the lesion in 5 to 10 per cent of the cases in which it is used. Bleeding is best controlled by vaginal pack until the adequacy of the biopsy material can be determined. Since carcinoma is detected in 51 per cent of the Group 3 (suspicious) smears, I wish to stress the need for particular care in obtaining adequate biopsy material from this group of patients.

From the pathologist's point of view, surgical conization with the cold knife is by far the most satisfactory method of obtaining a specimen that will explain abnormal cells in the cervical smear. It gives the pathologist the greatest amount of material to work with. It removes all of the tissue from an area that might conceivably harbor a small focus that could not be detected by the usual punch biopsy.

The surgeon, however, must realize that this procedure is not infallible and that the cone must be handled with great respect in order to preserve the surface epithelium intact. Carcinoma cells are not as cohesive as normal epithelium, and overzealous scrubbing and wiping of the external os should be avoided. The tenaculum and forceps should not touch the external os, and the cone should be so handled that all of the surface epithelium is preserved. One way to insure this is to deliver the cone into the hands of the pathologist with the mucous plug still intact in the external os. At this institution the cone is taken directly from the operating room to the laboratory, where twelve or more serial blocks made from it include the squamocolumnar juncture,

which has been identified with Lugol's solution. Twelve or more fresh frozen sections are made on the freezing microtome and examined immediately for carcinoma. If infiltrating carcinoma is present, the surgeon may proceed with a Wertheim hysterectomy. If carcinoma *in situ* is present, the surgeon usually performs a vaginal hysterectomy.

When the original sections are made from the cone, great care is taken to observe the epithelium at the outer fringes of the cone to determine whether the lesion extends out onto the portio vaginalis. If it does, and the surgeon has cut through an area of carcinoma, he is notified at once. After removal of the uterus, the vaginal cuffs are checked by the pathologist to insure that the lesion has been completely removed before the surgeon completes the repair.

In cases in which surgical conizing biopsy is all that is contemplated, it is essential that the apex in the endocervical canal as well as the fringe of the cone be carefully examined to eliminate the possibility of extension beyond the confines of the cone. My colleagues and I have had several experiences in which lesions extended wide out onto the lateral walls of the vagina, and others in which the process extended high in the endocervical canal. In 2 instances, early in our experience, examination of the vaginal cuff was neglected, and vaginal smears of both patients later demonstrated suspicious-appearing or malignant cells. In both instances the tissue removed at operation was rechecked and an extension to the line of excision demonstrated.

*Interpretation of Results.* — The third and perhaps the most difficult avenue of approach concerns the problem of interpretation.

The term "preclinical carcinoma" is a more fitting term for the invisible lesions of the cervix than the more conventional term "carcinoma *in situ*." Despite the fact that gynecologists at the clinic are keenly interested in preclinical carcinoma and aware of its importance, 56, or approximately 10 per cent, of the preclinical lesions observed here have proved to be infiltrating carcinoma.

Precisely what constitutes infiltrating carcinoma of the cervix has long been a debatable point. Theoretically and by definition it means the violation of the basement membrane of the mucosa by the carcinoma. From a practical standpoint, however, it is not so simple. In many carcinomas *in situ* varying degrees of involvement of the endocervical glands are demonstrated in the area of the squamocolumnar juncture. A number of investigators in the past have considered glandular involvement indicative of early invasion; at present, however, it is apparently rather widely accepted as a component of an *in situ* lesion.

The criteria for a diagnosis of infiltration are as follows: (1) a distinct break in the basement membrane, with infiltration of malignant cells into the lamina propria; (2) plugs of carcinoma cells deep to the endocervical glands that have caused a scirrhous reaction in the surrounding stoma, and (3) clusters of malignant cells in obvious vascular spaces, usually lymphatics. In general my colleagues and I are rather conservative when considering debatable infiltration and tend to err on the side of considering the lesion to be *in situ*. Since 1948, 441 carcinomas *in situ* of the cervix have been treated by some one of several conservative surgical methods, and so far as is known no lesion has metastasized. The 2 local recurrences in the vagina, mentioned previously, were explained by unrecognizable *in situ* spread onto the portio and surrounding vaginal cuff.

Carcinoma *in situ* of the cervix, in my opinion, is a surface carcinoma that sooner or later may develop invasive tendencies

and the ability to metastasize. It is not the purpose of this discussion to debate the pros and cons concerning the validity of carcinoma *in situ*. Anyone engaged in a screening-smear program should be actively engaged also in the interpretation of biopsy material and, in so doing, satisfy himself that he is dealing with a significant lesion. Furthermore, I am convinced that the physician who is not thoroughly familiar with tissue diagnosis is at a distinct disadvantage in interpreting cytologic signs in smears from the cervix.

Unfortunately, many questions concerning the validity of surface carcinoma cannot be answered. For example, if one elects to follow a patient by smear alone without tissue confirmation, the presence of malignant cells in the smear is not an acceptable basis for a diagnosis of bona fide carcinoma *in situ*. Conversely, if confirmation is obtained by biopsy and afterward the smear becomes negative, there is no proof that the lesion was not entirely removed in the biopsy specimen.

From the standpoint of pathologists, patients harboring carcinoma *in situ* while pregnant probably have bona fide lesions. In the past, numerous investigators have questioned the significance of epithelial cervical changes associated with pregnancy. It is not my purpose to discuss this rather specialized and isolated facet of carcinoma *in situ*. It has been the clinic's experience, however, that bona fide examples of carcinoma *in situ* occurring during pregnancy will most probably be observed also as residual lesions after the delivery of the child. In the clinic's series of carcinomas *in situ* there were 8 patients who were pregnant at the time of the initial smear and biopsy. In 3 of these patients residual carcinoma was observed three to five months post partum, when vaginal hysterectomies were done. Two patients, who were young and desired additional pregnancies, were treated by thorough cauterization after confirmation of the diagnosis by biopsy, and 1 patient underwent removal of a biopsy specimen from the cervix, by conization. The seventh patient had associated tubal pregnancy and underwent vaginal hysterectomy, and the eighth woman had early infiltrating carcinoma at the time of conizing biopsy, four months post partum. It seems, therefore, that carcinoma *in situ* exists in pregnancy, and our criteria for that diagnosis are the same as for the non-pregnant woman.

*Lesion Suspected From Smear but No Lesion at Biopsy (False "Suspicious" Smears).* — The problem of the falsely suspected smear has always concerned those engaged in the cytodetection of preclinical carcinoma. The pathologist, who is responsible for the tissue diagnosis as well as for the report of the smear, has a distinct advantage in assaying this problem. In the last analysis the adequacy of the biopsy material can best be evaluated in the laboratory, with specific reference to the amount of epithelium on the biopsy specimen and its location with regard to the squamocolumnar juncture. In order to maintain a successful program, the close cooperation of the gynecologist, the surgeon and the pathologist is essential. It is distinctly advantageous to be able to compare the cellular aberrations in the cervical epithelium with the atypical cells in the cervical smear in order to appreciate their origin and significance.

To illustrate this phase of the problem, all of the cases in which smears were suspected falsely for the past three years were reviewed (Table 3). In 37 of 96 cases reviewed the smears were considered true "false suspicious" smears. This means that apparently adequate sampling of the squamocolumnar juncture failed to reveal any significant cellular aberration bordering on dysplasia or basal cell hyperplasia. As cautery was frequently employed after the negative pathologic report had been

established, follow-up studies of these patients will probably be of doubtful significance; long-range plans, however, include them.

Basal cell hyperplasia was encountered in 12 of the 96 cases. This change in itself may produce atypical cells in the smear, depending on whether the process has reached the surface of the epithelium. Dysplasia, which could be confused with carcinoma *in situ*, was not demonstrated in any of the 12 cases. Biopsy material from 44 cervices demonstrated distinct dysplasia in part or in all of the material examined. In these cases great care must be exercised, on examination of tissue, not to exclude a small area of neoplasia that is situated adjacent to the dysplastic tissue. Microscopic sections should be cut at several levels of this material, and comparison of the exfoliative cells in the smear and on the surface epithelium in the section is extremely helpful in arriving at the conclusion that a satisfactory biopsy has been accomplished. Because atypical changes in the epithelium are frequently associated with overt carcinoma *in situ*, conization seems the most satisfactory method of obtaining material for examination of the squamocolumnar juncture.

In a rare case a decidual reaction may be encountered in the cervix that will tend to confuse the cytologist. In my experience approximately 62 per cent of false "suspicious" smears actually mirrored some degree of epithelial atypism short of carcinoma *in situ* that was present in the cervix at the time the smear was taken.

During the same three-year period, 41 smears were never satisfactorily explained. In reviewing the records it was noted that in 16 of these cases biopsy was a failure, in 8 cone failures occurred, and 17 patients either refused biopsy or returned to their homes for biopsy and definitive treatment. The biopsy failures occurred primarily in patients in whom the external os was small but office punch biopsy was attempted. The inadequate or unsatisfactory conizing biopsy may be the result of technical difficulties, rough handling, probing or dilatation of the external os at the time of operation, with loss of the surface epithelium.

*Treatment.*—Treatment of patients with carcinoma *in situ* has consisted mainly of vaginal hysterectomy or total abdominal hysterectomy, depending on the opinion of the consulting gynecologist. Twenty patients were treated with radium because of contraindications to surgical procedures. Seventeen of the proved carcinomas *in situ* have been treated by local methods: 7 by removal of the biopsy specimen and cautery alone and 10 by conization and cautery. All of the 17 patients were young women who desired families and who were willing to undergo frequent checkups for any abnormality in the cervical epithelium.

## SUMMARY

The detection of preclinical carcinoma of the uterine cervix requires close cooperation between the gynecologist, the surgeon and the pathologist. In the Mayo Clinic the detection rate of preclinical carcinoma of the cervix in the 66,511 primary cervical smears screened was 7.8 per 1,000 patients. The false "suspicious" rate was approximately 2.4 per 1,000 women screened. In nearly two-thirds of this latter group the biopsy material revealed the source of the atypical cells mirrored in the smear. The rate of incidence of carcinoma *in situ* detected in repeated cervical smears was a fourth that in the primary smears screened.

Extreme care is needed in obtaining biopsy material from the squamocolumnar juncture and in preserving the surface epithelium at the time of biopsy. The pathologist's role in preferential handling of such material and the use of fresh-frozen

sections as a diagnostic method have been stressed. It is advantageous to make the pathologist responsible for both the cytologic diagnosis and the tissue diagnosis. Infiltrating carcinoma was encountered in slightly over 10 per cent of preclinical cancers of the cervix detected by cervical smear at the Mayo Clinic.

ZUSAMMENFASSUNG

Die Entdeckung eines präklinischen Kollumkarzinoms erfordert eine enge Zusammenarbeit des Gynäkologen, des Chirurgen und des Pathologen. In der Erfahrung des Verfassers betrug das Verhältnis der Entdeckung eines präklinischen Kollumkarzinoms 7,8 per 1000 bei 66 511 primären Abstrichen aus dem Gebärmutterhals. Die Rate falscher "verdächtiger" Fälle betrug etwa 2,4 per 1000 bei den zur Aussiebung der Fälle untersuchten Frauen. In fast zwei Dritteln dieser letzten Gruppe enthüllte das Probeexzisionsmaterial die Quelle untypischer Zellen, die sich im Abstrich nachweisen liessen. Das Vorkommen von durch wiederholte Gebärmutterhalsabstriche entdecktem Carcinoma *in situ* betrug etwa den vierten Teil von den durch die ersten Abstriche ausgesiebten Fällen.

Zur Gewinnung von Probeexzisionsmaterial aus der Übergangsstelle vom Schuppenepithel zum Zylinderepithel und zur Erhaltung des oberflächlichen Epithels zur Zeit der Entnahme ist grösste Sorgfalt erforderlich. Die Rolle des Pathologen bei der besonderen Behandlung solchen Materials und bei der Anwendung frischer Gefrierschnitte zur Diagnose wird hervorgehoben. Es empfiehlt sich, dem Pathologen die Verantwortung sowohl für die zytologische als auch für die Gewebsdiagnose zu überlassen. Ein infiltrierendes Karzinom wurde in etwas über 10 Prozent von präklinischen Kollumkarzinomen mit Hilfe des Gebärmutterhalsabstriches in der Mayo Klinik entdeckt.

SUMARIO

A descoberta do carcinoma pre-clínico do colo uterino requer estreita cooperação entre o ginecologista o cirurgião e o patologista. Na experiencia do A. 66.511 especimens examinados revelaram 7.8 por mil dos pacientes. Os casos suspeitos foram de 2.4 por mil de mulheres examinadas. Em 2/3 do ultimo grupo a biópsia revelou a fonte de celulas atipicas encontradas no esfregaço. A constatação de carcinoma in situ em esfregaços repetidos foi de ¼ do que foi obtido nos esfregaços primariamente examinados. Extremo cuidado é necessario para obter material na biópsia da junção escamo-colunar preservando o epitelio durante a colheita. Acentua a preferencia do patologista por tal material e o uso de cortes congelados como métodos de diagnostico. É vantajoso entregar ao patologista a responsabilidade pelo diagnostico citologico e pelo histologico. O carcinoma infiltrante foi encontrado em pouco mais de 10% dos canceres preclínicos do colo uterino revelados pelo exame do esfregaço na Mayo Clinic.

RÉSUMÉ

La détection du carcinome du col de l'utérus au stade préclinique exige une collaboration étroite entre le gynécologue, le chirurgien et l'anatomopathologiste. Sur 66.511 frottis le diagnostic préclinique a pu être posé dans 7.8 0/00 des cas. Le pourcentage des cas "suspects" erronés a été d'environ 2.4 0/00. Dans près des deux tiers de ce dernier groupe le matériel de biopsie a révélé la présence de cellules atypiques (frottis). Le pourcentage de carcinomes in situ décelés au cours d'examens répétés des frottis du col a été d'un quart inférieur à celui des premiers frottis examinés.

L'obtention du matériel de biopsie à la limite de l'épithélium pavimenteux exige une technique délicate. L'importance de coupes fraîches congelées est soulignée. L'anatomopathologiste devrait accorder une attention particuliére à de tels examens, car il peut être rendu responsable à la fois du diagnostic cytologique et du diagnostic tissulaire. Le carcinome infiltrant du col a été rencontré dans un peu plus de 10% des cancers précliniques du col décelés par frottis à la Mayo Clinic.

RIASSUNTO

Il riconoscimento dello stadio pre-clinico del carcinoma del collo uterino richiede una stretta collaborazione fra il ginecologo, il chirurgo e l'anatomopatologo. L'esperienza dell'autore in questo campo si compendia in 66.511 strisci di secreto vaginale nei quali si ebbe il 7,8 per mille di reperti positivi per cancro. La percentuale dei casi sospetti fu del 2,4 per mille. In circa i due terzi di quest'ultimo gruppo la biopsia rivelò poi la presenza del cancro. La positività aumenta di un quarto se gli strisci vengono ripetuti più volte.

Si deve avere la massima sura quando si eseguono i prelievi al punto di passaggio fra epitelio pavimentoso e cilindrico. Oltre allo striscio cervicale, comunque, è bene che l'anatomopatologo esamini anche il materiale bioptico su sezioni istologiche.

Nel 10% dei casi di cancro pre-clinico svelato con gli strisci cervicali esisteva un carcinoma infiltrante.

RESUMEN

La detección del carcinoma del cuello del útero en la fase preclínica requiere una estrecha cooperación entre el cirujano, el ginecólogo y el anatomopatólogo. De acuerdo con la experiencia del autor, la cifra de detección preclínica del carcinoma del cuello del útero en 66,511 exudados cervicales examinados fué de 7'8 por cada 1.000 pacientes.

La proporción de frecuencia del carcinoma in situ reconocido en exudados cervicales repetidos fúe la cuarta parte de los primeros exudados.

Se debe tener extremo cuidado en la obtención de biopsia de la unión escamocolumnar, evitando dañar la superficie epitelial al hacerla. Es muy importante el papel del anatomopatólogo en el manejo de tal material y en el uso de cortes de congelación recientes para los diagnósticos.

Es ventajosos hacer al anatomopatólogo responsable del diagnóstico citológico y del diagnóstico tisular.

En la clínica Mayo se ha podido reconocer el carcinoma infiltrante del cuello de útero preclinicamente en algo más del 10% de los casos.

# Simple Laminectomy for Spondylolisthesis Without Spinal Fusion

ROBERT DEAN WOOLSEY, M.D., F.A.C.S.

ST. LOUIS, MISSOURI

THE term "spondylolysis" is derived from two Greek words; *spondylos*, meaning spine, and *lysis*, meaning loosening or solution. The term spondylolisthesis is a combination of *spondylos* with *listhesis*, meaning slipping and falling—in this case, slipping and falling forward. Persons with spondylolisthesis usually have spondylolysis associated with forward slipping of the body of the vertebra. This spondylolysis refers to the isthmus, or portion of the posterior element of the vertebra that attaches to the vertebral pedicle. In other words, slipping forward of the body of the vertebra is usually accompanied by a fibrous isthmus or pars interarticularis. The fibrous isthmus or spondylolysis may occur without the forward slipping of the vertebral body and is usually designated by the term "prespondylolisthesis" or "grade 1 spondylolisthesis."

The cause of these abnormalities has not been determined, but they are usually considered congenital. Their incidence varies but is usually stated as about 5 per cent of the general population.

The number of patients for whom these abnormalities become symptomatic is minimal. Nevertheless, such conditions must always be considered in the differential diagnosis of any condition involving low back pain and sciatica. The roentgen diagnosis of spondylolysis or fibrous isthmus can be made only by taking oblique views of the spine in addition to the conventional anteroposterior and lateral views. This is demonstrated in Figures 1 and 2.

My interest in the causative mechanism of the neurologic symptoms and signs of spondylolysis and spondylolisthesis began in 1950 with the following case:

*History.*—Mrs. C. E., a 69-year-old woman, was admitted to the hospital on Jan. 11, 1950.

Fig. 1.—Oblique views of lumbar portion of spine. Fibrous isthmus at fifth lumbar segment bilaterally.

Submitted for publication Nov. 3, 1957.

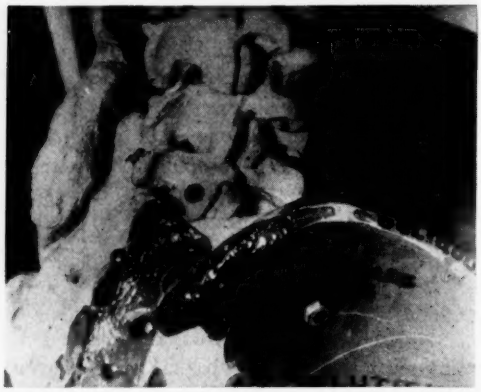


Fig. 2.—Skeleton turned in oblique view, demonstrating isthmus defect at fifth lumbar level.

Her chief complaint was of shooting pain in the left leg since May 1940, when she had had a fall. Afterward there were low back pain and bilateral sciatic pain, more marked on the left, particularly on walking. During the few weeks preceding hospitalization she had noticed some numbness of the lateral aspects of the legs and some weakness of dorsiflexion of both lower extremities.

*Examination.*—Bilateral limitation of forward bending and of straight leg raising was noted. Hypesthesia was present over the outer aspect of both calves and the dorsum of the foot. Weakness of dorsiflexion of both feet was noted, and ankle and knee jerks were absent.

Roentgenographic examination of the spine showed pronounced spondylolisthesis, with 1 cm. of anterior vertebral displacement of the fifth lumbar on the first sacral vertebra. Moderately advanced osteoarthritis was also observed. A myelogram showed no abnormalities.

*Operation.*—On Jan. 20, 1950, an incision was made over the fourth and fifth lumbar and first sacral spines, and the muscles were separated free bilaterally to the extent of the articulating facets. The spine and lamina of the fifth lumbar vertebra were freely movable, and the isthmus was obviously fibrous. Accordingly, the ligaments holding the lower facets were incised and the spine and lamina of the fifth lumbar vertebra removed. The pedicles were carefully dissected, so that the nerve roots at the fifth lumbar and the first sacral level were completely decompressed into the root canals.

Since discharge from the hospital on Jan. 30, the patient has been relatively free of pain and other symptoms.

*Results.*—Since January 1950, 36 patients in similar cases have been operated upon in similar fashion (Fig. 3).

Eleven of these patients were classed as having prespondylolisthesis or spondylolysis (Fig. 1). Twenty others were classed as having spondylolisthesis with spondylolysis. Three patients with myelographic evidence of ruptured intervertebral disks also had spondylolysis, and at operation the fifth lumbar arch and facets were removed, together with the involved nucleus pulposus (see table). The pedicles were dissected bilaterally to insure freedom of the fifth lumbar and first sacral nerve roots.

Two fusions were done by orthopedic surgeons. In a 17-year-old boy with Grade 4 spondylolisthesis, fusion was effected after removal of the posterior elements. The second fusion was performed in an adult with spondylolisthesis of the fourth on the fifth lumbar vertebra after simple laminectomy had failed to relieve his pain. This is the only patient operated upon for whom the original operation is rated as a failure. One other patient is considered to show only a fair result. The results of simple laminectomy are considered good after follow-ups ranging from three months to six years.

## COMMENT

The symptoms of spondylolisthesis are low back pain, often combined with unilateral or bilateral sciatica. Instability of the fifth lumbar vertebra, with progressive forward slipping, is considered the cause of the symptoms and signs encountered in these patients. Rupture of the intervertebral disk is frequently blamed for sciatica when this symptom is prominent. The physical signs are usually radicular

and involve the fifth lumbar and first sacral roots unilaterally or bilaterally. Occasionally there is hypesthesia involving the lateral aspect of the calf and foot. The ankle jerk may be absent. Atrophy of the calf is not common but may occur.

Instability of the fifth lumbar vertebra is not sufficient to explain this group of symptoms and signs. Many persons have known spondylolisthesis with no symptoms of any kind. Progressive slipping demonstrated roentgenographically is a rarity. The degree of forward slipping has little relation to the severity of the symptoms and signs. I have observed severe back pain, sciatica, hypesthesia of the fifth lumbar and first sacral dermatomes and absence of the ankle jerk in a person with prespondylolisthesis. Three patients have had a disk rupture associated with a fibrous isthmus or prespondylolisthesis, but there was no question of the diagnosis in their cases; the history, physical and myelographic signs were all definitely indicative of herniation of the nucleus pulposus.

On the basis of so-called instability, fusion of the lumbosacral joint has been the treatment of choice for spondylolisthesis. This treatment has had many drawbacks. In the first place, the lumbosacral joint is a difficult area in which to obtain good fusion. Some authors indicate that the incidence of pseudarthrosis is as high as 50 per cent. Fusion is a long-drawn-out procedure for the patient, both physically and economically. The results are poor in many instances, even when fusion is adequate. Many persons whose symptoms and signs indicate that benefit could be obtained from surgical therapy are not even considered for a fusion operation because of the magnitude of the procedure. Gill[1] has reported his results with an operative procedure exactly similar to that described in the cases here reported. He has used this procedure independently since 1950.

James and Nisbett[2] in 1953, writing of their posterior intervertebral body fusion of the lumbar portion of the spine for

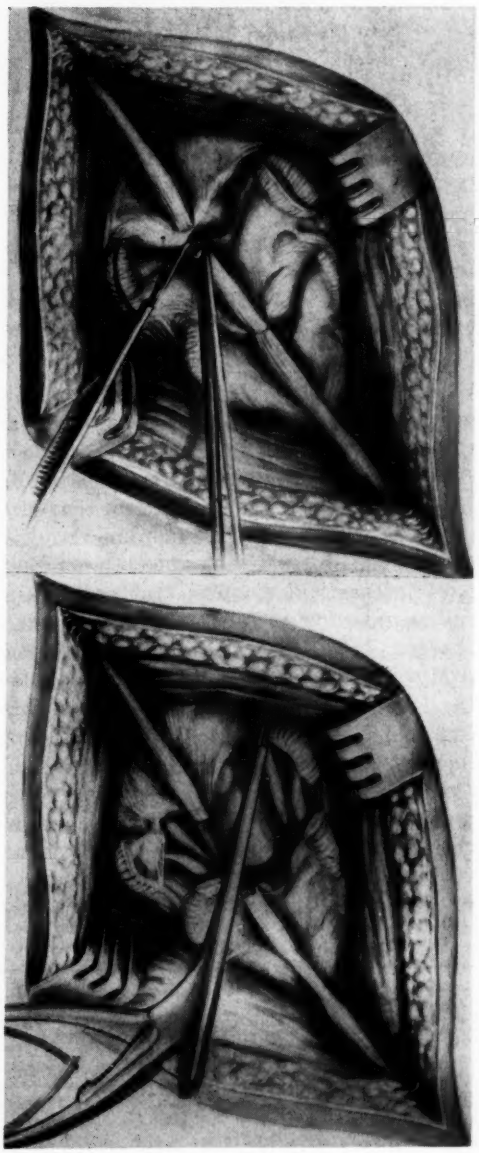


Fig. 3.—*Above*, dissection of lamina and spine of the fifth lumbar vertebra, including facets. *Below*, laminectomy completed, with fifth lumbar and first sacral nerve roots completely free.

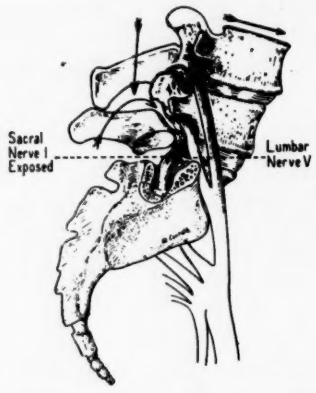



Fig. 4.—Diagram of relation of movable fifth lumbar lamina to fifth lumbar and first sacral nerve roots.

spondylolisthesis, mentioned a patient whose separated neural arch was excised without any other treatment. A good result ensued. These men were convinced, as were Gill and his co-workers, that the movable fifth lumbar spine and lamina and the ensuing reaction about the fibrous pars interarticularis was the mechanism responsible for the symptoms and signs observed in patients with spondylolisthesis.

My experience with both spondylolisthesis and prespondylolisthesis bears this out, and I see no reason for spinal fusion in most instances.

How is the sudden onset of symptoms and signs to be explained? In my opinion, the lamina and spine of the fifth lumbar vertebra have been attached to the pedicles at the pars interarticularis by fibrous union that is adequate to prevent movement of the lamina until some comparatively trivial injury occurs, usually in hyperextension or hyperflexion. From this time on the lamina and spine become freely movable on the pedicles, with resulting reaction at the pars interarticularis and impingement on the fifth lumbar and first sacral nerve roots (Fig. 4). This last factor is highly important. At operation, removal of the loose lamina and spine should be accompanied by careful dissection of the accumulation of fibrous and cartilaginous tissue on the medial side of the pedicles of the fifth lumbar, sufficient to make certain the freedom of the fifth lumbar and the first sacral nerve roots.

| | *Results* | |
|---|---|---|
| *Simple Laminectomy* | *Number* | *Result* |
| Prespondylolisthesis (spondylolysis) | 11 | Good |
| Spondylolisthesis | 20 | Good |
| | 1 | Fair |
| | 1 | Failure |
| Prespondylolisthesis with ruptured disk | 3 | Good |
| Fusion | 2 | Good |

## CONCLUSION

Thirty-six patients with various degrees of spondylolisthesis have undergone removal of the neural arch and spine, with dissection of both pedicles of the fifth lumbar vertebra. The results are encouraging and indicate that fusion is rarely necessary. Patients with prespondylolisthesis only are likewise relieved of back pain and sciatica by this technic. Since the results of simple laminectomy are usually good, fusion should be reserved for those patients who are not relieved by simple laminectomy. In such cases fusion can easily be done as a secondary procedure. In this series fusion has been done in 2 patients, with satisfactory results.

## CONCLUSIONS

Trente-six malades atteints de spondylolisthésis à des degrés divers ont subi l'ablation de l'arc nerveux et de l'arc vertébral de l'épine, avec dissection des deux racines de la 5e vertèbre lombaire. Les résultats de cette technique sont encouragents et montrent qu'une spondylosyndèse est rarement nécessaire. Elle soulage également de leurs douleurs dorsales les malades atteints de

préspondylolisthésis et de sciatique. Les résultats d'une laminectomie simple étant en général bons, la spondylosyndèse devrait être réservée aux cas ou la laminectomie simple s'avère insuffisante; elle peut être facilement pratiquée comme second temps opératoire. Les auteurs ont ainsi obtenu d'excellents résultats dans deux cas.


CONCLUSAO

Apresenta 36 pacientes com varios graus de espondilolistese que foram submetidos a remoção do arco neural e da coluna com dissecção dos pedículos da 5a. vertebra lombar.

Os resultados são animadores e indicam que a fusão é raramente necessaria. Os doentes com pre-espondilolistese apenas são tambem aliviados de dores lombares e da ciática por essa técnica.

Considerando que os resultados da simples laminectomia são usualmente bons deve ser reservada a fusão para os casos rebeldes. Nesses casos a fusão pode ser realizada como método secundario. Nesta serie dois pacientes foram submetidos á fusão com resultados satisfatorios.

CONCLUSIONI

Trentasei pazienti con spondilolistesi di varia gravità furono sottoposti all'asportazione dell'arco vertebrale e dell'apofisi spinosa e alla dissezione di entrambi i peduncoli della quinta vertebra lombare. I risultati sono soddisfacenti e indicano che la fusione non sempre è necessaria. Questa tecnica toglie il dolore dorsale e sciatico negli stadi pre-spondilolistesici. Poichè la semplice laminectomia dà buoni risultati, si deve riservare l'artrodesi a quei pazienti in cui la laminectomia abbia fallito.

Nella serie presentata l'artrodesi è stata fatta con buoni risultati in due casi.

SCHLUSSFOLGERUNGEN

Sechsunddreissig Kranke wurden wegen Wirbelverschiebungen verschiedenen Grades mit Entfernung des Wirbelbogens und des Dornfortsatzes und Durchschneidung beider Wirbelbogenhälse des fünften Lendenwirbels behandelt. Die Erfolge sind ermutigend und deuten darauf hin, dass eine Fusion nur selten nötig ist.

Auch Kranke, die nur unter einer Anlage zur Wirbelverschiebung leiden, können durch dieses Verfahren von ihren Rücken- und Ischiasschmerzen befreit werden. Angesichts der gewöhnlich guten Ergebnisse der einfachen Laminektomie sollte die Fusion für diejenigen Kranken reserviert bleiben, die durch die einfache Laminektomie nicht geheilt werden. In solchen Fällen lässt sich die Fusion als zweite Operation leicht durchführen. In der vorliegenden Krankenserie wurde die Fusion an zwei Patienten ausgeführt; die Resultate waren zufriedenstellend.


REFERENCES


1. Gill, G. G.; Manning, J. G., and White, H. L.: Surgical Treatment of Spondylolisthesis without Spine Fusion. Excision of the Loose Lamina with Decompression of the Nerve Roots, J. Bone and Joint Surg. 37-A:493-520, (June) 1955.

2. James, A. and Nisbet, N. W.: Posterior Intervertebral Fusion of the Lumbar Spine, J. Bone & Joint Surg. 35-B:181-187, (May) 1953.

# Pollicization of the Index Finger

## Report of a Case

TIMOTHY A. LAMPHIER, M.D., F.A.C.S., F.I.C.S., D.A.B.
AND
MALVIN F. WHITE, M.D., D.M.D.*
BOSTON, MASSACHUSETTS

THE problem of the amputated thumb is magnified, especially when the major hand is concerned. Certainly, in the young man or woman who earns a living with his or her hands, this disability is one of great concern. Without question, there should be offered to this person the possibility of substituting, by surgical means, the index finger for the lost thumb.

Since the thumb controls 40 per cent of the function of the hand, its replacement is of paramount importance. Functionally, all of the remaining fingers together total only 60 per cent. As Moore[1] stated, "Loss of a thumb is a crippling injury, only equalled perhaps by the loss of all the fingers of a hand."

Our main object is to restore lost prehensile ability. In subtotal amputation of the thumb at the metacarpophalangeal joint, the powerful thenar muscles are present but cannot be utilized.

Workers, whether in skilled or unskilled trades, require the pinching action of the thumb with the remaining digits in order to carry out any form of work requiring manual dexterity. The technic to be described in this paper is a subtotal reconstruction of the thumb by transposing the index finger when the metacarpal bone of the thumb is still intact. The long finger assumes the important function of the index finger.

*Department of Surgery, St. Elizabeth's Hospital, Brighton, Massachusetts, and at Beth Israel Hospital, Boston: Associate Clinical Professor of Plastic Surgery at Tufts Medical School.
Submitted for publication Oct. 1, 1957.

As Littler[2] has so well emphasized, "the three elements pertinent to useful function are, (1) sensation, (2) stability and (3) independence of motion." This end result can be accomplished by a one-stage transfer of a segment of the index finger.

"Preservation of stereognosis, fingernail and general cosmetic value is the aim of the surgeon, together with retaining as much as possible the over-all length of the digit."[3]

Fig. 1.—Kidde-Robbins tourniquet. This assures complete control of blood flow, an important factor during arm and leg operations. Pressure is regulated by a control knob which can be preset to the desired dial reading (0 to 1000 mm. of mercury). This desired pressure is maintained absolutely constant until changed by turning the control knob or released by pushing the on-off switch. There is no danger of loss of pressure even if the Freon container is removed or changed during the operation. Freon is nontoxic and noninflammable.

In our opinion, transposition of the index finger is superior to simple deepening of the first metacarpal cleft, because the reconstructed thumb more closely resembles its amputated predecessor in length, function, action, usefulness and stability.

As opposed to total loss of the thumb, the metacarpal, with its intrinsic musculature, is intact, which adds greatly to the stability of the transferred digit. Furthermore, this type of amputation is the commoner type so often observed in industry, i.e., at the articulation of the metacarpal and the proximal phalanx. The advantage of subtotal reconstruction is that it can be carried out in one stage, whereas total reconstruction requires two or three stages.

Technically speaking, the most important part of the procedure is maintenance of the neurovascular supply. In the case to be described, both lateral components of the nerve and blood supply to be transplanted were preserved. Plastic skin flaps must be provided for, so that they do not limit function.

Finger motion is encouraged as soon as clinical osseous stability is gained.

To obtain the proper length of the transposed digit it must be shortened, so that, when opposed to the remaining fingers in

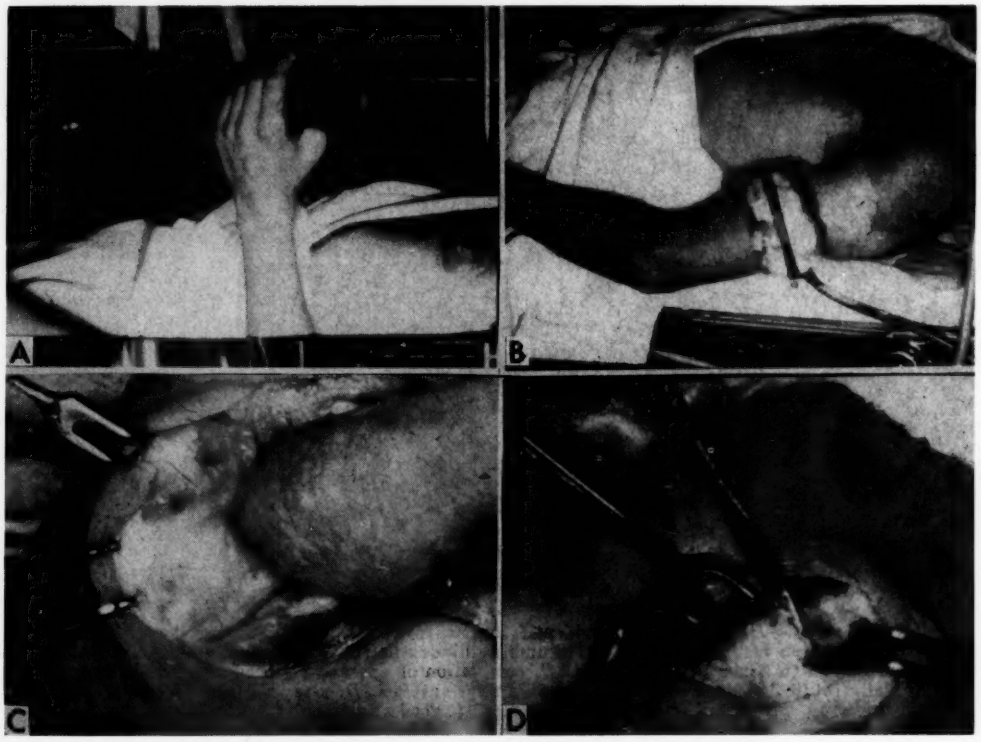



Fig. 2.—Photographs depicting, in step-by-step fashion, the procedure employed. *A*, amputated thumb at level of metacarpophalangeal joint. *B*, pneumatic tourniquet in place elevated to 300 mm. of mercury. *C*, elevation of dorsal skin flap opposite base of index finger. *D*, transection of metacarpal bone of index finger at juncture of its proximal and middle thirds. (*Continued next page*)

Fig. 2 (*continued*).—*E*, black silk loop identifying neurovascular bundle during deepening of interdigital cleft between amputated stump of thumb and index finger. *F*, anastamosis of flexor digitorum profundus tendon to flexor pollicis longus. *G*, completion of operative procedure. Transplanted index finger axially rotated 90 degrees, into place. Skin flaps sutured. *H*, x-ray showing section of Kirschner wire transfixing bone fragments. *I*, good functional end result.

flexion, it will not extend beyond them. In addition to axial rotation of 90 degrees, a large cleft must be provided to allow for sufficient abduction and opposition.

A step omitted in the procedure to be described, which might have been valu-

able, is the use of an intramedullary bone graft or peg to unite the transferred digit with the metacarpal of the thumb.

The digital nerve trunk supplying adjacent sides of the long and index fingers must be split high into the base of the hand and the blood supply dissected free, so that transposition can be completed. Although tendons can be preserved in the procedure we followed, they were divided and anastomosed to the extensor and flexor tendons of the amputation stump.

## REPORT OF CASE

M. R., a 34-year-old white man was employed as a mill hand by a manufacturer of furniture. At the time of injury the patient was rounding the leg of a chair with a "shaper" when the leg kicked back and the knife of the shaper amputated his left thumb and severely lacerated the anterior aspect of his left hand. He was first taken to the office of a physician, where emergency treatment was given to control hemorrhage. He was then admitted to the hospital, and we were called for consultation.

Examination revealed that, in the region of the distal interphalangeal joint of the left thumb, the thumb had been completely amputated except for a small section of skin. Just distal to the metacarpophalangeal joint of the thumb the bone was severely comminuted, and all of the soft tissues had been lacerated to such a degree that they were not viable. There was a laceration extending from the thenar eminence of the thumb proximally to the left wrist. There was a small laceration measuring 1 inch (2.5 cm.), midway in the region of the web space between the index and the long finger. There was a third laceration, approximately 2 inches (5 cm.) in length, following the proximal palmar crease from the radial aspect of the left hand over its volar surface.

The patient was immediately taken to the operating room, where amputation of the left thumb at the metacarpophalangeal joint was completed, the multiple long involved lacerations were sutured, and foreign bodies (wood, etc.), as well as comminuted bone, were removed as follows: With adequate pentothal anesthesia and with a tourniquet about the upper part of the left arm, the left hand was thoroughly washed with septisol and irrigated with 1,000 units of saline solution. The distal stump of the thumb was debrided. Plastic skin flaps were then prepared to cover what was left of the stump of the thumb, and these flaps were approximated with interrupted black silk sutures, as were also the involved multiple lacerations involving the palm of the left hand and the thenar eminence. A petrolatum dry sterile dressing was then applied, and the patient was returned to the ward in good condition. The wounds healed well by primary intention, and there were no complications.

Six weeks later, the following procedure was performed: With the patient under combined brachial block supplemented by general anesthesia, an incision was made through the skin, encircling the proximal interphalangeal region of the left index finger. The extensor tendons, the flexor tendons and the main arterial veins and nerves supplying the middle and distal phalanges were preserved intact. These two phalanges, together with their attached structures, were then separated from the remaining proximal portion of the phalanx by disarticulation.

A pedicle graft of the interdigital space between the base of the thumb and the base of the index finger was outlined and elevated. With careful dissection, the proximal portion of the tendons, blood vessels and nerves to the distal portion of the index finger were preserved down to the hand itself. The proximal phalanx of the index finger and the distal half of the second metacarpal bone were then removed after the metacarpal had been severed through. This gave sufficient laxity to all the soft tissue structures attached to the distal portion of the index finger to permit the transposition.

A portion of the web that was devoid of skin was then covered with a full thickness free skin graft dissected from the amputated portion of the finger. The proximal portion of the middle phalanx of the index finger was rongeured so that the cartilage was entirely removed. This was then fixed by a Kirschner wire to the small remaining proximal phalanx of the amputation stump of the thumb. The tendons were transplanted to the extensor and flexor tendons of the thumb. The tourniquet was released. Bleeding vessels were tied with No. 40 plain catgut.

The margins of the skin were closed with interrupted No. 40 black silk. Dry sterile dress-

ings were applied over the graft site. The web between the thumb and index finger and the position of the new thumb were maintained by means of a plaster of paris cast.


## SUMMARY

The cosmetic loss involved in the narrowing of the palm from pollicization is far outweighed by the gain of a new opposable thumb that allows the hand to function as a unit. The procedure described provides for a strong grip with powerful opposition, and the new thumb has normal sensation. The interdigital cleft must be deepened between the index and long fingers to provide for easy opposition.

As in the case here reported, a pollicized digit will be cyanotic for several hours after the operation before it regains its usual color.

From a technical aspect, the most important step in the procedure is preservation of the neurovascular bundle of the transplanted index finger.

A technical step omitted by the authors, which is of great value in these procedures, is the use of an intramedullary bone graft to maintain axial rotation of the transplanted finger at an angle of 90 degrees and to face the remaining fingers.

Of prime importance is the maintenance of a bloodless field by the application of a pneumatic tourniquet, e. g., the Kidde-Robbins tourniquet. Skin flaps must be allowed for, to provide proper cutaneous suturing without tension. The hand is maintained in a plaster cast for eight to twelve weeks, and early motion is instituted.

A case is reported in detail, in which a subtotal reconstruction of the thumb was performed, the index finger being used as a transposed digit. The advantages of this method as regards total rehabilitation of an injured major hand are described.*


*A sound motion picture (in color) of this procedure is available through the American Cyanamid Co., Danbury, Connecticut.


## RÉSUMÉ

L'effet inesthétique résultant de la constriction palmaire après reconstruction d'un pouce est largement compensé par l'acquisition d'un nouveau pouce opposable permettant à la main de retrouver son unité fonctionnelle. La technique ici décrite permet une forte préhension, et la sensibilité du pouce reconstruit est normale. Les espaces interdigitaux doivent être agrandis entre l'index, le médius et l'annulaire en vue d'une bonne opposition.

Comme dans le cas décrit, le doigt reconstruit reste cyanotique pendant plusieurs heures après l'opération, avant de reprendre une coloration normale.

Il est essentiel de préserver le faisceau neurovasculaire de l'index transplanté. Un point technique de grande valeur, est l'utilisation d'une greffe osseuse intramédullaire afin de maintenir la rotation axiale du doigt transplanté à un angle de 90°.

Il est de pemière importance aussi de maintenir le champ opératoire exsangue par l'application d'un tourniquet pneumatique.

La suture cutanée doit se faire sans tension. La main est maintenue dans un plâtre pendant huit à douze semaines. Des exercises précoses sont à recommander.

Les auteurs décrivent un cas détaillé, énumérant les avantages de cette méthode de reconstruction du pouce en utilisant l'index.

## ZUSAMMENFASSUNG

Die kosmetische Einbusse, die bei der Herstellung eines neuen Daumens mit der Verengung der Hand einhergeht, wird durch den Gewinn eines neuen Daumens, der Opposition und eine einheitliche Funktion der Hand gestattet, bei weitem ausgeglichen. Die hier beschriebene Methode führt zu einem festen Griff der Hand mit

kräftiger Oppositionsfähigkeit; der neue Daumen hat ein normales Gefühlsvermögen. Der Spalt zwischen dem Zeigefinger und dem Mittelfinger muss vertieft werden, um eine leichte Opposition zu gestatten.

Der zum Daumen umgewandelte Zeigefinger wird für mehrere Stunden nach der Operation zyanotisch und gewinnt dann seine normale Farbe wieder, was auch in dem hier berichteten Falle geschah.

Vom technischen Standpunkt aus gesehen liegt der wichtigste Schritt des operativen Vorgangs in der Erhaltung des Nervengefässbündels des transplantierten Zeigefingers. Ein wichtiger technischer Schritt, der bei diesen Verfahren von grossem Wert ist und von den Verfassern ausgelassen wird, ist die Verwendung eines intramedullären Knochentransplantats zur Erhaltung der axialen Rotation des transplantierten Fingers bei einem Winkel von 90 Grad und zur Gegenüberstellung gegen die anderen Finger.

Von grösster Wichtigkeit ist die Erhaltung eines blutlosen Operationsfeldes durch Anwendung einer luftgefüllten Staubinde. Es muss für ausreichende Hautlappen gesorgt werden, um sorgfältige Hautnähte ohne Spannung zu ermöglichen. Die Hand wird 8 bis 12 Wochen lang in einem Gipsverband getragen, und frühzeitige Bewegung wird eingeleitet.

Es wird über einen Fall im einzelnen berichtet, in dem eine subtotale Wiederherstellung des Daumens ausgeführt wurde. Der Zeigefinger wurde als transponiertes Glied benützt. Die Vorzüge des Verfahrens im Hinblick auf die völlige Wiederherstellung einer schwer verletzten Hand werden beschrieben.

RIASSUNTO

La menomazione estetica conseguente alla riduzione di superficie del palmo della mano in seguito alla pollicizzazione del 2° dito è di gran lunga compensata dal vantagio di avere un pollice opponibile che restituisce alla mano la sua piena funzione. Il metodo descritto consente di ottenere una valida presa, una efficace opposizione e un nuovo pollice con sensibilità normale. Lo spazio interdigitale fra l'indice e il medio viene approfondito in modo da ottenere una opposizione facile.

Il dito pollicizzato rimane cianotico per alcune ore dopo l'intervento, poi riprende il suo colore normale. Il punto più importante della tecnica è rappresentato dal rispetto del fascio neuro-vascolare dell'indice. Grande valore è attribuito all'impiego di un trapianto osseo intra-midollare che consente di mantenere la rotazione assiale del dito trapiantato a un angolo di 90 gradi, così da potersi contrapporre alle altre dita.

Di grande importanza è anche il poter mantenere il campo esangue con l'applicazione di un laccio pneumatico; i lembi cutanei debbono essere suturati senza tensione; la mano è mantenuta in gesso per 8-12 settimane e mobilizzata precocemente

Viche descritto un caso in cui si fece la ricostruzione sub-totale del pollice usando l'indice.

SUMARIO

O prejuiso estético que ocorre no estreitamento da região palmar pela perda do polegar é superada pela policização que fornece um polegar novo apto para oposição permitindo usar a mão como uma unidade funcional. O método descrito pelos autores provê uma garra com oposição potente dando ao novo polegar sensação normal. A comissura interdigital deve ser aprofundada entre o indicador e os dedos longos para opsição mais facil.

Como no caso aqui apresentado deve existir cianose do dedo policisado por algumas horas antes que ele recupera a côr usual. Do ponto de vista técnico o tempo

mais importante no método é a preservação do feixo neuro-vascular do dedo transplantado.

Um tempo que foi omitido pelos AA. mas que é de grande valor é o uso de um enxêrto intramedular com ôsso para manter a rotação axial em 90° para fazer oposiçao dos demais dedos.

De máxima importância é conseguir um campo exangue pelo uso de um torniquête pneumático. Os retalhos de pele devem estar preparados para revestir sem sutura tensas. A mão é mantida engessada por 8-12 semanas com movimentação precoce á seguir. Apresentam e descrevem um caso com reconstrução subtotal do polegar usando a transposição de dedo. Descrevem as vantagens desse método, para reconstrução total de uma lesão grave da mão.


RESUMEN

La pérdida estética que representa el estrechamiento de la palma en la polización de un dedo se ve ampliamente compensada por la ventaja que supone un nuevo pulgar oponente que permite a la mano funcionar unitariamente.

El procedimiento aquí descrito proporciona una fuerte presa con oposición y conserva una buena sensibilidad La abertura interdigital debe practicarse entre los dedos índice y medio para proporcionar una oposición fácil.

Como en el caso presente el dedo pulgarizado permanecerá varias horas cianótico antes de recuperar su color natural.

Desde el punto de vista técnico lo más importante es la conservación de los pedículos neurovasculares en el dedo transplantado. Un detalle técnico de gran importancia, auque omitido en este caso por los autores, es la colocación de un injerto óseo intramedular para mantener la rotación exial del dedo transplantado en un ángulo de 90 grados mirando a los otros dedos.

Es primordial trabajar en campo exangüe por medio de un torniquete. Pueden ser aconsejables colgajos cutáneos para que la sutura pueda llevarse a cabo sin tensión. La mano debe mantenerse escayolada de ocho a diez semanas instituyendo pronto la movilización.

Los autores describen un caso suyo en el cual se reconstruyó parcialmente el pulgar utilizado el dedo índice. Se describen las ventajas del método en su relación con la rehabilitación total de las lesiones graves de la mano.


REFERENCES


1. Moore, F. T.: Pollicisation of the Index Finger, Brit. J. Plast. Surg. 1:60, 1948.
2. Littler, J. W.: Subtotal Reconstruction of the Thumb, Plast. Reconstruct. Surg. 10:215, 1952.
3. Nemethi, C. E.: The Primary Repair of Traumatic Digital Skeletal Losses by Phalangeal Recession, J. Bone & Joint Surg. 37-A:78, 1955.

# Surgery of the Thyroid and Parathyroids

## Hyperparathyroidism

IRVING L. LICHTENSTEIN, M.D., F.A.C.S., F.I.C.S., D.A.B.
AND
MARVIN S. LEVY, M.D., F.A.C.P., D.A.B.
BEVERLY HILLS, CALIFORNIA

IN 1925, Mandl, a Viennese surgeon, first removed a parathyroid adenoma from a patient with osteitis fibrosa cystica.[1] This followed Schlagenhaufer's suggestion in 1915 that enlargement of a parathyroid associated with osteitis fibrosa cystica could not be secondary to the bone disease, since it involved only one gland. It has been only within the past ten to fifteen years, however, that the significance of the urogenital system in the diagnosis of hyperparathyroidism has been established. Indeed, Oliver Cope and others pointed out that renal calculi are more common as a manifestation of this condition than is bone disease itself.[2] It has been suggested that anywhere from 2 to 4 per cent of all patients with renal lithiasis are suffering from primary hyperparathyroidism. In 1956, Janelli classified all pathologic conditions of the parathyroid that had been recorded up to that time.[3]

I. Primary hyperparathyroidism, due to:
   - A. Functional parathyroid adenoma
     1. Single
     2. Multiple
   - B. Diffuse parathyroid hyperplasia

II. Carcinoma of the parathyroid glands
   - A. Functional (primary hyperparathyroidism)
   - B. Nonfunctional

III. Secondary parathyroid hyperplasia, due to:
   - A. Chronic renal insufficiency
   - B. Vitamin D deficiency
   - C. Rickets
   - D. Multiple myeloma
   - E. Osteomalacia
   - F. Paget's disease

IV. Cysts of the parathyroid glands

V. Nonfunctioning parathyroid adenoma

VI. Hypoparathyroidism
   - A. Surgical tetany
   - B. Secondary, due to:
     1. Hemorrhage
     2. Tuberculosis
     3. Amyloidosis
     4. Syphilis
     5. Infarction
   - C. Idiopathic hypoparathyroidism
     1. Congenital absence of the glands
     2. Congenital hypoplasia secondary to maternal hyperparathyroidism

VII. Primary parathyroid atrophy

VIII. Pseudohypoparathyroidism, a genetic disorder.

Primary surgical interest in the foregoing classification resides, however, in

Read at a meeting of the Regional Division of the United States Section, International College of Surgeons, Las Vegas, Nevada, April 1957.
Submitted for publication Oct. 20, 1957.

primary hyperparathyroidism, carcinoma of the parathyroid glands and hypoparathyroidism. The last is of interest to the surgeon only insofar as it may be a surgical complication following operation on either the thyroid or the parathyroids.

*Physiologic Aspects.* — Normally, the production of parathormone is stimulated by altered serum calcium levels. Albright suggested that the primary action of parathormone is on the renal tubule, causing a lowered renal threshold for phosphorus excretion.[4] This results in a fall of serum phosphorus, which in turn results in an elevation of serum calcium, which is liberated from the calcium phosphate of bone. This in turn is followed by increased calcium excretion. Classically, then, in the presence of hyperparathyroidism one observes elevated values for calcium in the serum and in the urine, an increased level of phosphorus in the urine but a depressed concentration of phosphorus in the serum. With deposition of calcium in the kidney, renal insufficiency eventually develops. The resulting phosphorus retention encourages a lowering of the blood calcium level. It is obvious how confusion may arise from the actual reversal of values for calcium and phosphorus in a case of hyperparathyroidism associated with kidney disease. It is clinically important to remember that the action of parathormone on the skeletal system may be mitigated by a high calcium diet. Therapeutically, parathormone has only limited usefulness, since tolerance to the drug develops rapidly.

*Anatomic and Embryologic Aspects.* — It is incumbent upon the surgeon who explores the neck to familiarize himself with the embryologic and anatomic character of the parathyroid structures if exploration is to be successful. The inferior parathyroids arise from the endoderm of the third pharyngeal pouch, while the superior parathyroids arise from the fourth pouch. Because the inferior parathyroids have so far to migrate caudally with the thymus they show the greatest variance in position. They may separate themselves from the thymus anywhere along its route of migration and have been observed from the anterior mediastinum up to the angle of the mandible. On occasion they may be discovered within the thymus gland itself. There is considerably less variation in the position of the superior parathyroid glands, which are ordinarily located near the upper third of the thyroid lobes on their posterior aspect. They are found at a point where the recurrent laryngeal nerve passes under the lowest fibers of the inferior constrictor muscle as it is attached to the horn of the thyroid cartilage. For adequate visualization of these glands it is usually necessary to sever the superior pole and lift it off of the constrictor muscle.[5] As the blood supply of parathyroid glands located in the posterior mediastinum always arises from the inferior thyroid artery, it has been concluded that these are errors of mechanical displacement rather than embryologic defects, since in the latter the blood supply may arise from immediately adjacent structures.[6] There are ordinarily four symmetrically placed parathyroid glands, although the number can range anywhere from one to ten. Gilmour and Martin observed more than four glands in approximately 6 per cent of 527 necropsy cases, and fewer than four in 14 per cent of cases. They emphasized that two glands may be fused together and then appear more than twice normal size.[7] Ordinarily they are approximately 0.5 cm. wide and 1.5 cm. long and receive their blood from a branch of the inferior thyroid artery. They are ovoid and are frequently differentiated from fat, thyroid or thymic tissue or lymph nodes only with considerable experience. Particularly is this true of the lower glands. The yellow brown color, the at-

TABLE 1.—*Signs and Symptoms of Hyperparathyroidism*

| |
|---|
| 1. Skeletal |
| a. Bone and joint pain ± fractures |
| b. Giant cell tumors |
| 2. Renal |
| a. Calculi and infections |
| b. Polyuria and polydipsia |
| General |
| a. Hypertension |
| b. Abdominal and intestinal disorders |
| c. Headache, fatigue and hypotonicity |
| d. Concomitant endocrine adenomas |

TABLE 2.—*Laboratory Data in Cases of Hyperparathyroidism*

| |
|---|
| 1. Serum |
| Calcium ↑ phosphorus ↓ ; alkaline phosphatase ↑ proteins normal |
| 2. Urine |
| Calcium ↑ ; phosphorus ↑ |

TABLE 3.—*Diagnosis of Masked Hyperparathyroidism*

| |
|---|
| 1. Calcium restriction |
| 100-200 mg. calcium diet, 1 week > 24-hour urinary calcium > 150 mg. |
| 2. Renal tubular phosphate resorption |
| $\%\ \text{TRP} \left\{ \frac{\text{urine } PO_4 \text{ serum creatinine}}{\text{urine creatinine serum } PO_4} \right\} \times 100 = \downarrow$ |

tached fatty tissue and the fine vascular network entering the hilum of the gland just beneath a glistening capsule are helpful macroscopic aids. Nevertheless, despite assertions to the contrary,[8] the average surgeon will have considerable difficulty in positive identification of all the glands unless he utilizes frozen section examinations of minute biopsy specimens, for verification.

*Primary Hyperparathyroidism.* — The symptoms of this condition are caused by the elevated serum calcium level, the pathologic changes in the genitourinary tract or those of the skeletal system (Table 1).

The symptoms resulting from the neuromuscular depression caused by elevated calcium values are vague and include lassitude, gastrointestinal symptoms (abdominal pain, constipation, ulcers, vomiting) and weakness.

Abnormalities in the skeletal system, namely, osteitis fibrosa cystica and less commonly osteoporosis, may give rise to pathologic fractures (30 to 40 per cent of cases).[9] The maxilla is frequently the first site of cystic change. Epulis is common. Resorption of the lamina dura about the teeth has been suggested as one of the earliest roentgenographic signs of all pathologic changes associated with this condition.

Nephrolithiasis and chronic renal damage give rise to well-known symptom complexes. One must always be alert to differentiate preoperatively primary hyperparathyroidism associated with secondary renal disease and secondary hyperparathyroidism which is a compensatory result of renal failure. There is general agreement among investigators than in the vast majority of cases hyperparathyroidism is detected because of renal lithiasis or nephrocalculosis. At least 70 per cent of patients with hyperparathyroidism have renal disease.[10] Renal insufficiency with polyuria, polydipsia and hypertension are frequently encountered.

Adenomas, easily the commonest cause of primary hyperparathyroidism, develop in the lower parathyroid glands in 80 per cent of the cases. This is an important observation from a surgical point of view. Although multiple adenomas have been reported, Norris suggested that these may not be valid and that parathyroid hyperplasia secondary to renal damage should be suspected in all such instances.[11] Recorded adenomas have ranged in weight from 0.5 to 120 Gm., the average being approximately 12 Gm. and the mean weight 7 Gm. There seems to be some direct correlation between the size of the adenoma

and the serum calcuim concentration; with extremely large tumors, however, this relation is often invalid.[12] Generally, too, the length of time that a patient has had a hyperfunctioning adenoma is more important in the production of its effect than is its size.[5]

Carcinomas of the parathyroid are noteworthy from a surgical aspect because of their rarity (only 23 acceptably documented cases have been reported): their size (ordinarily larger than adenomas and frequently palpable), and the fact that histologic differentiation from benign adenoma is frequently impossible by the present day technics, so that metastatic deposits into lungs, liver and kidneys are frequently indistinguishable microscopically from their benign counterpart. Unlike malignant disease of the thyroid, parathyroid carcinomas are usually functional. There is an excellent possibility that they arise from preexisting adenomas. Parathyroid carcinoma is diagnosed on discovering evidence of invasion at operation, lymph node involvement, distant metastases or the eventual course of the patient, rather than by the pathologic picture, which can be extremely deceptive. The most bizarre-appearing adenoma with cytologic characteristics of malignancy, including nuclear variations and/or hyperchromatism, may be benign, and vice versa.[11] It is therefore incumbent upon the surgeon, before he attempts to eradicate the primary source of spread (radical neck dissection, etc.) to be certain of diagnosis. It is wiser to be conservative if there is any doubt, and await future developments in the clinical course. Roentgen therapy has been valueless for this disease.

Primary parathyroid hyperplasia involving all the glands produces the same symptoms as adenoma or carcinoma. In cases of true primary hyperplasia an attempt should be made to leave no more than 200 mg. of viable parathyroid tissue. It would appear significant, however, that calcification in the urinary tract has been present in every recorded case of parathyroid hyperplasia.

TABLE 4.—*Surgical Treatment of Parathyroids*

1. Thyroid incision
2. Division of pretracheal muscles
3. Traction sutures in thyroid lobe
4. Traction ligature on inferior thyroid artery
5. Identification of
   a. recurrent laryngeal nerve
   b. inferior parathyroid gland
   c. twigs of artery leading to anomalous positions
6. Identification of superior parathyroid gland
7. Investigation of
   a. carotid sheath
   b. retroesophageal area
   c. mediastinum
8. Exploration of opposite side
9. Biopsy of glands
10. Consideration of thyroid biopsy*

*Sternum should not be split.

TABLE 5.—*Treatment of Postoperative Hypoparathyroidism*

1. Acute (with tetany)
   100 cc. 10% gluconate in 1,000 cc. dextrose in N/2 saline solution*
2. Chronic
   a. AT10, 1-3 cc. daily till 3 + Sulkowitch reaction obtained, then 1 cc. 3 times weekly
   b. Vitamin $D_2$, 50,000-300,000 units daily
   c. Aluminum hydroxide, 30 cc. 4 times daily
   d. Calcium lactate, 10 Gm. orally 3 times daily

*Parathormone generally ineffective.

*Secondary Hyperparathyroidism.*—This is of interest to the surgeon only that he must differentiate it from primary hyperthyroidism. This differential diagnosis may be impossible when primary hyperparathyroidism is associated with advanced renal damage from calcification. When this occurs there is phosphorus retention and later calcium depression. These serum chemical alterations are characteristic also of secondary hyper-

parathyroidism and may resist differentiation. "Renal rickets" is secondary hyperparathyroidism subsequent to renal insufficiency occurring during a period of active bone growth in a child.

*Diagnosis of Primary Hyperparathyroidism (Table 2).*—The diagnosis must be confirmed before operation is undertaken. Elevation of the level of serum calcium is not adequate *per se* unless the dietary intake is strictly controlled and the laboratory values are reproducible. Elevated levels are associated with many other conditions, the more common of which are multiple myeloma, prostatic carcinoma, hyperproteinemia and hypervitamin D therapeusis. With advanced renal damage secondary to primary hyperparathyroidism, serum calcium levels may be even lower than normal because of phosphate retention. Howard has suggested that primary hyperparathyroidism is the only abnormal state that leaves unaltered the normal cerebrospinal fluid level of calcium (4.5 to 5.5 mg. per hundred cubic centimeters[18]). There is apparently a cerebrospinal block which behaves differently toward the hypercalcemia of hyperparathyroidism and the elevated serum calcium levels of other pathologic conditions. In all other hypercalcemic states the calcium level in the spinal fluid is elevated.

*A. Hypercalcemia*: It should be remembered that calcium is present in both the ionic and the protein bound form (albumin). Normally about 55 per cent of the serum calcium is in ionic form. This is the fraction which is affected by the action of parathormone. Clearly then, in a patient with a subnormal protein level a total calcium value that is ordinarily in the top normal range may be an indication of parathyroid overactivity (Fig. 1).[4] In other words, with a protein value of 5 Gm. per hundred cubic centimeters, a total calcium content of 10.5 mg. per hundred cubic centimeters would be well within hyperparathyroid levels (normal adult value for calcium, 9.5 to 10.5 mg. per hundred cubic centimeters).

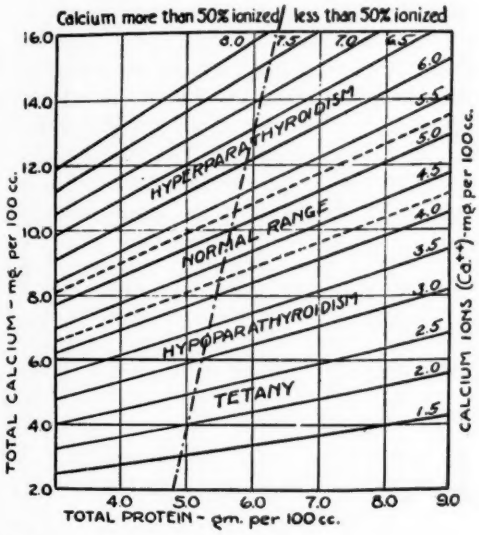



Fig. 1.—Nomogram reveals calcium ion concentration if total protein and calcium values of serum are known. (McLean, and Hastings, Am. J. M. Sc. 181:601, 1935.)

*B. Hypophosphatemia*: In the absence of renal impairment with phosphorus retention, a lowered value for serum phosphorus is probably the most significant sign of hyperparathyroidism. Nevertheless, lowered phosphorus levels may also be associated with secondary hyperparathyroidism, as well as with vitamin D intoxication (normal adult values, 2.5 to 4 mg. per hundred cubic centimeters). In the presence of renal insufficiency, the decrease of serum phosphorus may be obscured by phosphorus retention, sometimes resulting even in hyperphosphatemia.

*C. Hypercalcinuria*: This may be a regular observation in many conditions associated with hypercalcemia and is not in itself diagnostic. The Sulkowitch test for calcium in the urine may give negative results in cases of hyperparathyroidism. A more

sensitive method is the quantitative evalution of twenty-four hours urinary calcium after the patient has been given a diet of 125 mg. calcium daily. Under these circumstances the excretion in the urine should be less than 100 mg. a day, for normally the urine carries one-third and the feces two-thirds of the daily calcium excretion.

*D. Hyperphosphaturia*: This test is rarely used by clinicians despite the fact that the increased excretion of phosphorus is probably a primary action of parathormone. It may well be that the future differential diagnosis between primary and secondary hyperparathyroidism will rest upon the determination of the urinary phosphorus level.

*E. Increased Serum Alkaline Phosphatase*: This occurs only when there is skeletal involvement in the disease. It is not diagnostic and occurs also with all osteoblastic metastatic carcinomas, osteogenic sarcomas, Paget's disease, obstructive jaundice, etc.

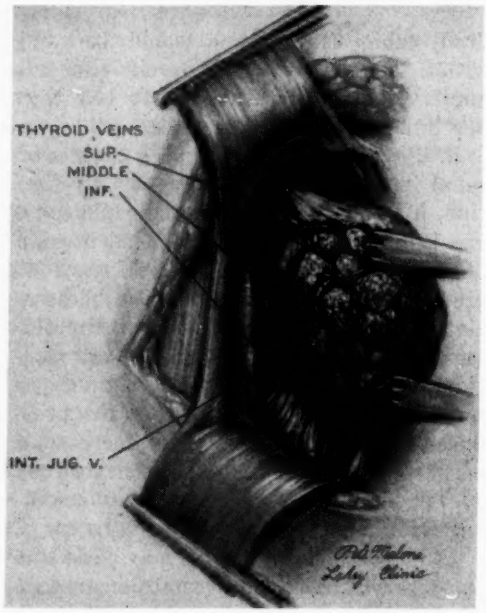



Fig. 2.—High division of ribbon muscles. Note that middle thyroid vein must be divided in order to gain access to inferior thyroid artery and recurrent laryngeal nerve. (Lahey, F. H.: Surg. Clin. North America 29:631, 1949.)

*F. Osseous Changes*: With hyperparathyroidism there are generalized decalcification, loss of trabecular structure and/or cystic changes. Although these conditions are not diagnostic, they are of considerable help in establishing the presence of hyperparathyroidism. Loss of the lamina dura, the bony cortex around the teeth, is allegedly one of the earliest roentgenologically demonstrable signs of demineralization in cases of hyperparathyroidism.

*G. Urinary Calcifications*: Nephrocalcinosis and/or lithiasis should always demand of the urologist a differentiation from hyperparathyroidism. Probably more cases of overactivity of the parathyroid gland are eventually picked because of symptoms reparable to the urinary tract than for any other reason. Significantly, the renal damage is ordinarily irreversible, and despite removal of the adenoma patients may eventually succumb to kidney failure.

*H. Recent Metabolic Tests for the Detection of Masked Hyperparathyroidism (Table 3)*: These studies are based on the fact that the primary action of parathyroid hormone is on the kidney. Interference with the tubular reabsorption of phosphate occurs, resulting in phosphaturia and hypophosphatemia. The decreased serum phosphorus encourages mobilization of phosphate and calcium from the bones and consequent hypercalcemia and hypercalcinuria. The increased concentration of calicum ions in the serum inhibits the production of further parathyroid hormone. These tests have not been observed over a sufficiently long period to enable one to assess their clinical value

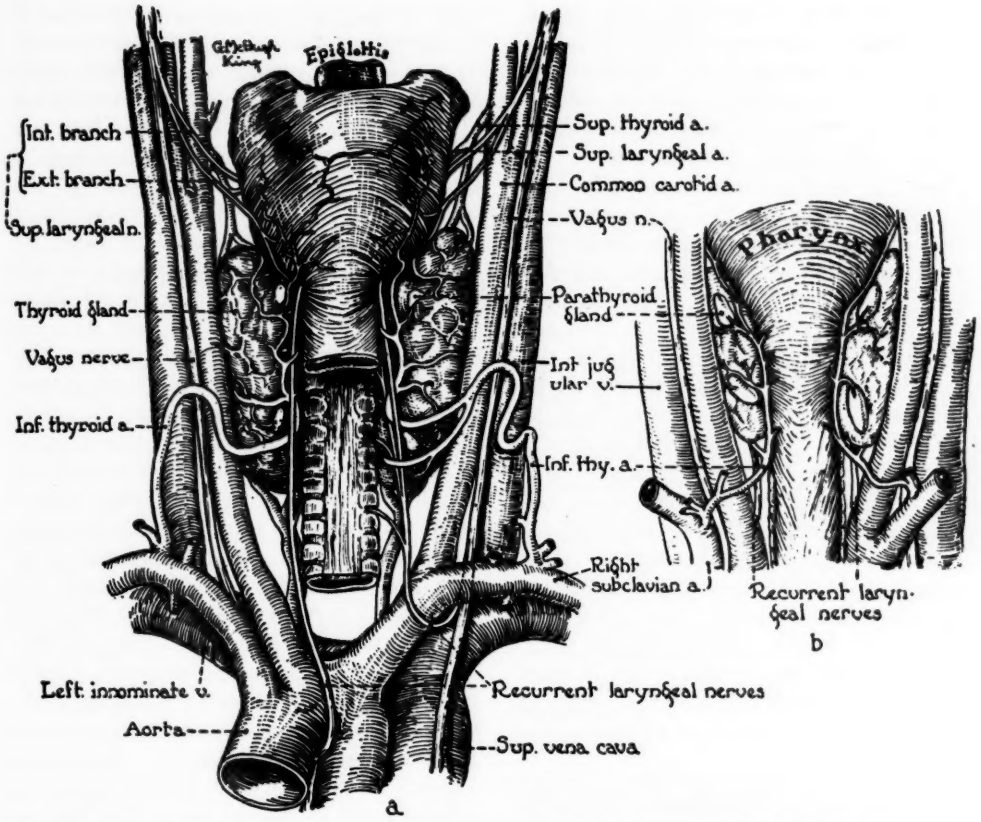



Fig. 3.—Posterior view of larynx, revealing true course of inferior thyroid arteries on left and inaccurate representation on right. (Nordland, Surg., Gynec. & Obst. 51:449, 1930.)

accurately.[15]

*1. Renal Tubular Phosphate Resorption.* This would logically be the most direct measure of parathyroid function. The test assumes that creatinine clearance is an accurate measure of the glomerular filtration rate. Normal is 91±3 per cent, with a pronounced depression in the presence of hyperparathyroidism. It must be recalled that intrinsic renal disease may affect the results.

*2. Calcium Infusion.* Since elevation of serum calcium ions inhibits parathyroid activity, the normal person will have hyperphosphatemia and hypophosphaturia. In the presence of an adenoma, however (an autonomous source of parathyroid hormone), the infusion of calcium should produce little or no change in the phosphorus levels of the serum or the urine.

*3. Phosphate Restriction.* The normal person on a restricted phosphate diet is able to conserve phosphate. In the presence of hyperparathyroidism this conservation is destroyed and phosphate loss continues.

*Surgical Treatment of Primary Hyperparathyroidism* (*Table 4*).—When one appreciates the frequent anomalous position of the parathyroids, the difficulty in iden-

tification of these glands and their small size, it becomes apparent that a detailed knowledge of anatomy and embryology, coupled with meticulous surgical dissection and perfect hemostasis, is necessary if a successful result is to ensue.

The usual thyroid incision is made. The skin and plastysma flaps are reflected above the thyroid notch and below to the suprasternal notch. The pretracheal muscles should be divided high in order to preserve the nervous innervation that enters these muscles in the lower portion of the neck (Fig. 2). The middle thyroid vein is divided. I have found it advantageous to identify the inferior artery as it emerges from behind the carotid sheath. A ligature is tied about this artery and used for traction. Difficulty may be encountered in identification of the vessel if one fails to remember that it courses cephalad before entering the gland and lies posterior to the carotid sheath (Fig. 3). The lobe of the thyroid gland is then mobilized by utilizing transfixion sutures through the parenchyma so as not to destroy the thyroid by crushing clamps. It is usually a simple matter at this point to identify the recurrent laryngeal nerve as it sweeps over or between the twigs of the inferior thyroid artery (Fig. 4). The inferior parathyroid gland should be easily discernible if one follows the branches of the inferior thyroid artery that supply it. Care should be taken to note the patterns of any anomalous twigs from the inferior thyroid artery leading into the mediastinum. This may give one a clue to aberrant parathyroid tissue. The superior pole of the thyroid gland is then divided and the gland retracted in a caudal direction. The superior parathyroid is usually located against the larynx approximately a third of the distance down from the superior pole. If both parathyroid glands have not been identified at this time, a search should be instituted about the carotid sheath, the retroesophageal area, and the posterior superior mediastinum. The infrathyroid tissue may be examined, but the anterior mediastinum cannot be adequately explored from above without danger. All glands located in the posterior mediastinum are supplied by a branch from the inferior mesenteric artery and should therefore be locatable by following these branches. Embryologic displacements into the anterior mediastinum, however, usually have their own blood supply. Parathyroid glands, it must be remembered, can be located anywhere from the angle of the mandible down to and including the superior mediastinum. In 10 per cent of reported cases the adenoma has been found in an aberrant position.

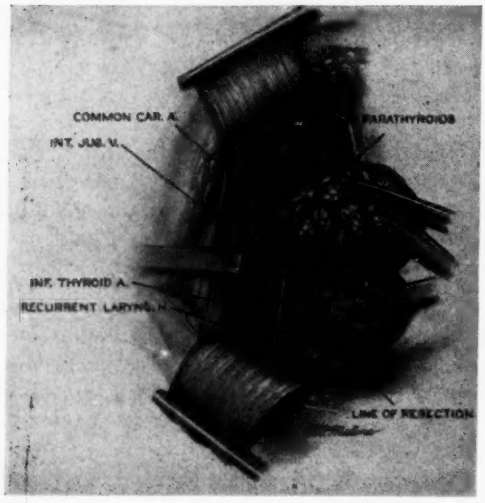



Fig. 4.—Traction sutures, rather than crushing clamps utilized with thyroidectomy, inserted to maneuver thyroid. (Lahey, F. H.: Surg. Clin. North America 29:631, 1949.)

At this point the surgeon should change position and perform the same thorough investigation on the opposite side. It is of great advantage to stand on the side of the table closest to the area of the neck that is being explored. One of several situations will now confront the surgeon.

If one of the glands in the neck is missing, a meticulous search of that particular area must ensue, and the adenoma will probably be found there. Biopsy of one of the identified glands should reveal atrophy if an adenoma is present elsewhere. Only a minute biopsy specimen need be taken, as a skilled pathologist can make such a diagnosis at frozen section. The services of an experienced pathologist are a *sine qua non* of the successful surgical treatment of parathyroid disease. If hyperplasia is noted in all the glands, the surgeon must then decide whether this is a secondary compensatory phenomenon or is true primary hyperparathyroidism. The services of a skilled endocrinologist at the operating table are again of inestimable value. With hyperplasia it has been suggested that three and one-half glands be resected, only 30 to 200 mg. of tissue in the remaining gland. One must be aware, however, at all times that even with atraumatic surgery and minimal biopsy a parathyroid gland may be destroyed through ischemia. Caution should be utilized too if an adenoma is found early in the exploration, since multiple adenomas have been reported in up to 10 per cent of cases.[6] This figure is probably much too high, however. If no adenoma has been demonstrated after this cautious search, palpation of the thyroid lobe should be carefully performed. Intrathyroid parathyroid nodules have been described (1 to 2 per cent of cases).[13] A subtotal thyroidectomy should be seriously considered if no adenoma is discovered even though no nodules are palpated. Some authors suggest longitudinal splitting of the gland, though it is difficult to understand how minute adenomas could be discovered grossly with such a procedure. The operation should be concluded at this time, as mediastinal exploration should be reserved for a later date. A substantial number of cases have been reported in which there was complete chemical and clinical cure of the patient and no definite adenoma was discovered on cervical exploration. The explanation is apparently that the exploration devascularized or inadvertently destroyed the adenoma. In any event, no further surgical intervention was necessary.

If after three months' observation and reevaluation of the patient's condition there is not adequate improvement, preparation should be made for mediastinotomy. This should be necessary in no more than 1 to 2 per cent of cases.[6]

From the midline to the third interspace an incision in the mediastinum is made in the form of an inverted V so that closure will aid in sternal mobilization. Exploration should extend down to the pericardium, with particular attention to the thymus gland because of its embryologic significance. The remnant thymus structure should be removed, and exploration should include all structures down to the lung roots and pleura. I have seen an adenoma within the thymus, and their occurrence has even been reported in the pericardial wall.[10] Wire is used to approximate the sternum. Since a normal parathyroid gland weighs from 30 to 40 mg., identification of an adenoma should not be too difficult, since the smallest recorded adenoma weighed 400 mg., or ten times the weight of the average parathyroid.

Postoperatively it must be remembered that in the presence of an adenoma the remaining glands are atrophic. Removal of the primary source of parathormone therefore results in transient postoperative tetany in the majority of cases. This is more severe in cases with skeletal involvement, since rapid resorption of calcium by the bones can be anticipated before the serum calcium returns to normal.

Manifestations of hypocalcemia are:

A. Increased neuromuscular irritability (acute)
   1. Corpopedal spasm and positive Trousseau sign
   2. Laryngeal spasm
   3. Epileptic seizures
   4. Paresthesias
   5. Positive Chvostek sign.

B. Increased deposition of calcium (chronic)
   1. Calcification of brain
   2. Cataracts
   3. Ridging of nails
   4. Increased density of bones.

Laboratory tests usually reveal (a) hypophosphaturia; (b) hyperphosphatemia; (c) hypocalcemia, and (d) hypocalcinuria.

The treatment of hypoparathyroidism (Table 5) must be considered from the standpoints of the acute and the chronic condition.

Calcium gluconate or chloride (10 cc. of 10 per cent solution), given intravenously, will be effective immediately, but its effect is of short duration. Care must be taken, when using calcium chloride, to avoid painful sloughs.

Parathormone, given subcutaneously in 2 cc. doses, will take effect less rapidly but will have a more prolonged action. Tolerance of the drug occurs, however, necessitating increasing doses for diminishing effect.

Vitamin D (100,000 to 400,000 units daily) and dihydrotachysterol (A. T. 10) have a delayed but prolonged effect. The former medicament is expensive and somewhat less effective than A. T. 10. The latter may be given as 5 to 10 cc. daily for a few days, then 1 to 3 cc. several times weekly, depending on the calcium levels.

Calcium lactate or chloride should be administered orally three times daily to insure a high calcium intake. Phosphorus ingestion should be decreased; this is why milk and cream are contraindicated.

Fractures and deformity have been noted in the postoperative period, and it has been suggested that orthopedic support and sometimes immobilization of the extremities be utilized in cases of severe skeletal involvement. Rarely, recalcification of the bones does not follow removal of hyperfunctioning parathyroid tissue. Conversely, however, renal damage is usually irreversible, though function may improve to some extent.

## SUMMARY AND CONCLUSIONS

The classification of parathyroid disease is reviewed as are its anatomic, physiologic and embryologic backgrounds. The clinical, metabolic and pathologic aspects of parathyroid hyperfunction are discussed. Differentiation between primary and secondary hyperparathyroidism is included.

The diagnosis and treatment of primary hyperparathyroidism is dealt with in detail. It is emphasized that all patients with renal calculi should be investigated for parathyroid dysfunction.

Surgical intervention is the only effective treatment for primary hyperparathyroidism. The surgeon must be familiar not only with the regional anatomic but with the embryologic, pathologic and physiologic aspects of the parathyroid glands. Cervical exploration should reveal the cause of primary hyperparathyroidism in 98 per cent of the cases.

Multiple adenomas and carcinomas of the parathyroids are rare.

The postoperative treatment of a patient who has undergone a parathyroid operation demands skill and patience. This is discussed in some detail.

The diagnosis of parathyroid disease can be established with reasonable certainty if care is exercised in choosing and

interpreting present-day chemical and metabolic tests.

The surgical treatment of parathyroid hyperfunction demands meticulousness, skill, determination and knowledge. The successful surgical result merits the time and energy expended in the diagnosis and treatment of this condition.

Parathyroid adenoma improperly treated can cause indefinite morbidity and mortality from renal damage. Sincere attempts to diagnose this condition will result in the salvage of many patients before the ravages of renal and skeletal disease become irreparable.

## RÉSUMÉ ET CONCLUSIONS

1. L'auteur décrit la classification, l'anatomie, la physiologie et l'embryologie de l'hyperparathyroïdisme.

2. Il en discute les aspects cliniques, métaboliques et pathologiques ainsi que le diagnostic différentiel entre l'hyperparathyroïdisme primaire et secondaire.

3. Le diagnostic et le traitement de l'hyperparathyroïdisme primaire sont commentés.

4. Tous les malades atteints de calculs rénaux devraient être soumis à un examen de la fonction parathyroïdienne.

5. La chirurgie est la seule thérapeutique efficace de l'hyperparathyroïdisme primaire, et le chirurgien doit connaitre à fond les aspects aussi bien anatomiques locaux qu'embryologiques, pathologiques et physiologiques des parathyroïdes.

6. L'exploration cervicale devrait révéler la cause de l'hyperparathyroïdisme primaire dans 98% des cas.

7. Les adénomes et carcinomes multiples des parathyroïdes sont rares.

8. Le traitement post-opératoire exige de l'adresse et de la patience. L'auteur s'étend sur ce point.

9. Le diagnostic peut être établi avec de bonnes chances d'exactitude par un choix judicieux et une bonne interprétation des tests chimiques et métaboliques.

10. Le traitement chirurgical de l'hyperfonction parathyroïdienne demande non seulement de l'habileté et de la minutie, mais des connaissances anatomiques approfondies et de la détermination. Les bons résultats que l'on obtient compensent largement le temps et l'énergie consacrés par le chirurgien.

11. Le diagnostic d'adénome de la parathyroïde est délicat, mais posé à temps il permet de sauver de nombreux malades avant les ravages irréversibles causés par les lésions rénales et osseuses.

## ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

1. Es wird ein Überblick über die Klassifizierung, die Anatomie, die Physiologie und die Embryologie der Erkrankungen der Nebenschilddrüse gegeben.

2. Die klinischen, metabolischen und pathologischen Grundzüge der Überfunktion der Nebenschilddrüse werden erörtert. Dazu gehört eine Unterscheidung zwischen primärer und sekundärer Überfunktion der Nebenschilddrüse.

3. Die Diagnose und Behandlung der primären Überfunktion der Nebenschilddrüse wird im einzelnen dargestellt.

4. Es wird hervorgehoben, dass alle Kranken mit Nierensteinen auf eine Funktionsstörung der Nebenschilddrüse untersucht werden sollten.

5. Die einzige wirksame Behandlung der primären Überfunktion der Nebenschilddrüse besteht im chirurgischen Eingriff. Der Chirurg muss nicht nur mit den örtlichen anatomischen sondern auch mit den embryologischen, pathologischen und physiologischen Eigenheiten der Nebenschilddrüse vertraut sein.

6. Die Explorierung des Halses sollte in 98% der Fälle die Ursache der primären

Überfunktion der Nebenschilddrüse aufklären.

7. Multiple Adenome und Krebse der Nebenschilddrüse sind selten.

8. Die postoperative Behandlung des Kranken nach einem Eingriff an der Nebenschilddrüse erfordert Erfahrung und Geduld. Auf diesen Punkt wird genauer eingegangen.

9. Die Diagnose einer Erkrankung der Nebenschilddrüse kann mit ziemlicher Sicherheit gestellt werden, wenn die Auswahl und die Auslegung der modernen chemischen und Stoffwechseluntersuchungen mit Vorsicht und Sorgfalt erfolgt.

10. Die chirurgische Behandlung der Überfunktion der Nebenschilddrüse erfordert Exaktheit, Erfahrung, Entschlussfähigkeit und W i s s e n. Die bei der Diagnostizierung und Behandlung dieser Erkrankung aufgewendete Zeit und Energie macht sich durch den erfolgreichen Ausgang des chirurgischen Eingriffs belohnt.

11. Die falsche Behandlung eines Adenoms der Nebenschilddrüse kann zu unabsehbarer Krankhaftigkeit und zum Tode infolge von Nierenschädigung führen. Ernsthafte Bemühungen, diese Krankheit zu erkennen, können viele Kranke vor den irreparablen Zerstörungen der Nieren und des Skeletts bewahren.


## SUMARIO E CONCLUSOES

1. O A. faz a revisão da anatomia, fisiologia, e embriologia das afecções paratiroideanas.

2. Discute os as pectos clinico, metabolico e da patologia da hiperfunção paratiroideana. Inclue menção para diferenciar os hiperparatireoidismo primário e secundário.

3. Apresenta em detalhe o diagnostico e tratamento.

4. Realça a necessidade de investigar calculose renal em todos os pacientes portadores de disturbios paratireódêos.

5. O único tratamento efectivo é o cirúrgico. O cirurgião deve conhecer a anatomia regional, a embriologia a fisiologia e a patologia da glândula.

6. A exploração cervical deve revelar a causa do hiperparatireoidismo em 98% dos casos.

7. Os adenomas múltiplos e os carcinomas são raros.

8. O paciente operado deve merecer cuidado e paciencia. Êste aspecto é discutido pormenorisadamente.

9. O diagnóstico pode ser estabelecido com razoavel certesa se utilisa e interpreta bem os testes quimicos e metabolicos.

10. O tratamento cirurgico da hiperfunção paratireoideana exige meticulosidade, habilidade determinação e cultura. O sucesso cirurgico depende do tempo e da energia dispendisos no diagnostico e no tratamento.

11. O adenoma paratireoidêo impropriamente tratado pode causar grande morbidade por dano renal. As tentativas bem orientadas para diagnosticar a molestia salvara muitos doentes antes que o dano renal e as lesões esqueléticas se tornam irreparaveis.



## RIASSUNTO E CONCLUSIONI

1. Rassegna dell'anatomia, fisiologia ed embriologia delle paratiroidi e classificazioni delle loro malattie.

2. Discussione degli aspetti clinici, metabolici e patologici degli iper-paratiroidism, distinguendoli in primitivi e secondari.

3. Elementi per la diagnosi e la cura dell'iper-paratiroidismo primitivo.

4. Tutti i malati con calcolosi renale devono essere studiati per un'eventuale disfunzione delle paratiroidi.

5. L'unico metodo di cura efficace è quello chirurgico; il chirurgo deve impra-

tichirsi non solo dell'anatomia della ghiandola, ma anche della sua embriologia, fisiologia e a anatomia patologica.

6. Nel 98% dei casi di iperparatiroidismo primitivo è possibile dimonstrarne la causa coll'esplorazione chirurgica del collo.

7. Gli adenomi multipli e i carcinomi della paratiroide sono rari.

8. La cura post-operatoria dopo paratiroidectomia richiede abilità e pazienza.

9. La diagnosi può essere stabilita con una certa sicurezza interpretando con cura i tests chimici e metabolici moderni.

10. La cura degli stati di iperfunzione richiede meticolosità, abilità e nozioni tecniche; i risultati che si ottengono compensano gli sforzi spesi per la diagnosi e la cura.

11. Un trattamento inadeguato di un adenoma paratiroideo può causare uno stato di malattia permanente e anche la morte per lesioni renali; una cura ben fatta può salvare invece i malati prima che le lesioni renali e scheletriche siano divenute irreversibili.

REFERENCES

1. Mandl, F.: Therapeutischer Versuch bei einem Falle von Obsteitis Fibrosa Generalisata mittels Exstirpation eines Epithelkoerperchen-tumors, Zntrlbl. Chir. 53:260, 1926. (Cited by Rienhoff, W. F.: Ann. Surg. 131:917, 1950.)

2. Cope, O.: Surgery of Hyperparathyroidism: The Occurrence of Parathyroids in the Anterior Mediastinum and the Division of Operation into Two Stages, Ann. Surg. 114:706, 1941.

3. Janelli, D. E.: The Parathyroid Glands, with Special Emphasis on Surgical Aspects, Surg. Gynec. & Obst. (Internat. Abstr.) 102:105, 1956.

4. Albright, F., and Reifenstein, E. C.: Parathyroid Glands and Metabolic Bone Disease. Baltimore: The Williams and Wilkins Company, 1948.

5. Lahey, F. H.: Parathyroid Tumors, Surg. Clin, North America 27:477, 1947.

6. Black, B. M.: Surgical Treatment of Hyperparathyroidism, Surg. Clin. North America 32:1031, 1952.

7. Gilmour, J. R., and Martin, W. J.: Weight of Parathyroid Glands, J. Path. & Bact. 44:431, 1937.

8. Lahey.[5] Black.[6]

9. Hoffman, G. T.: The Parathyroid Glands. Surg., Gynec. & Obst. (Internat. Abstr.) 95:417, 1952.

10. Black, B. M.: Surgical Aspects of Hyperparathyroidism, Surg., Gynec. & Obst. 89:172, 1948. Cope.[2]

11. Norris, E. H.: The Parathyroid, Adenoma, Surg. Gynec. & Obst. (Internat. Abstr.) 84:1, 1947. Carcinoma of the Parathyroid Glands. Surg. Gynec. & Obst. (Internat. Abstr.) 86:1, 1948.

12. Rienhoff, W. F.: The Surgical Treatment of Hyperparathyroidism. Ann. Surg. 131:917, 1950.

13. Howard, J. E.; Carey, R. C.; Rubin, P. S., and Levine, M.: Diagnostic Problems in Patients with Hypercalcemia, Tra. Assn. Am. Phys. 62:264, 1949.

14. McLean, F. C., and Hastings, A. B.: Clinical Estimation and Significance of Calcium Ion Concentration in the Blood, Am. J. M. Sci. 189:601, 1935.

15. Goldzieher, J. W.; Heaney, J. P., and Fairweather, M. J.: Problems in Diagnosis and Management of Functioning Parathyroid Tumors, J.A.M.A. 164:1054, 1957.

**Note to Our Contributors**

The Editorial Board takes pleasure in announcing that, beginning with the March issue, the Journal will assume the costs of engraving for three one-column copper halftones, or the equivalent thereof, for each article carrying illustrations, the height of these cuts to be determined by the Editorial Office.

No restriction, of course, is placed upon the number of illustrations the author wishes to include at his own expense, beyond the limits necessarily imposed by the length of the article.

# *Editorial*

## The Application of Cardiopulmonary Physiology

IT has become imperative to apply the results of cardiopulmonary physiologists to everyday clinical practice in dealing with cardiac and pulmonary disease. Surgeons are no longer interested in purely anatomic diagnosis; physiologic diagnosis is also important. This has prompted us to develop a complete cardiopulmonary laboratory under the auspices of a trained physiologist (Dr. Daneshvari). In so doing we hope to offer a service to our fellow practitioners, promoting better clinical concepts of the diagnosis and management of cardiac and pulmonary problems; determining the physiologic capacities of patients in these categories, and differentiating heart and lung problems.

Needless to say, adequate functional tests of pulmonary ventilation, cardiac evaluation, arterial blood oxygen saturation and carbon dioxide excretion, diffusion studies, electrocardiographic studies of the heart under stress and strain, plus adequate correlation with the clinical background and the history, will remove a great deal of clinical error and guesswork, gradually increasing understanding and perspective in this field. The proper diagnosis will be aproached more nearly, more accurate therapy will be applied and better management instituted, and the prognosis will have a higher proportion of accuracy.

It may be that in the near future every physician, whether general practitioner, internist, general surgeon, or thoracic surgeon, will rely extensively upon the trained cardiopulmonary physiologist.

*Information Derived from Cardiopulmonary Studies.—Dyspnea*: Dyspnea has become an increasingly important factor in medicine. We predict that its importance will increase further as the span of life increases.

The cause of shortness of breath is frequently obscure. It may be due to any of numerous causes, such as emphysema, pneumoconiosis, asthma, bronchospasm, lack of oxygen absorption, destruction of lung tissue, cardiac deficiency, coronary insufficiency, hysteria or neurosis.

Evaluation of the physiologic measurements of patients in any of these conditions can aid materially in the accurate clinical deductions drawn as to the cause, diagnosis, prognosis and proper therapy and management of the given condition.

In our opinion, the time has arrived when every cardiovascular and pulmonary problem should be studied in a scientific cardiopulmonary laboratory. It goes without saying that not only the mortality but the morbidity rates associated with these conditions are astounding. It is our hope that, with adequate understanding and management of these problems, some reduction in both death and illness will be effected. Prognosis can be greatly aided by more precise knowledge of the patient's cardiac and pulmonary status.

*Emphysema*, which has already been mentioned, is without question startling as to incidence, morbidity and mortality, requiring the utmost efforts toward accurate diagnosis, prognosis, management and therapy. Undoubtedly, life expectancy can be increased by an improved approach on a physiologic basis. Industrial appraisals of cause, disability and extent of disability may be helped in certain cases.

The correlation of pathologic changes in the heart and lungs with other systemic disease by adequate objective appraisal has definite value. The differentiation of cardiac and pulmonary disease is greatly aided by studies of cardiopulmonary function.

Determination of the functional capacity and exercise tolerance of patients with cardiac disease is valuable and necessary.

Proper physiologic studies of the heart and lungs may be important in the management of any major operation, enabling the surgeon to avoid pitfalls in the treatment of chronically ill patients, e.g., the hazards of acidosis and alkalosis.

Periodic reevaluation of patients with limited cardiac and pulmonary function may be of clinical interest; the proper study of cardiac surgical patients is absolutely necessary. This may include cardiac catheterization and cardiographic studies.

The study of patients under consideration for thoracic or pulmonary operations is without question greatly aided by proper analysis. This may emphasize the importance of conservation of lung tissue, altering the procedure radically and in some cases completely contraindicating surgical intervention.

Bronchospirometric studies are most valuable in the determination of the working capacity of each lung. An accurate estimate is made as to the percentage of minute ventilation, and oxygen uptake. The principal application of this, of course, is in consideration of either collapse or resectional therapy.

In the syndrome of obesity, which is considered a triad, i.e., alveolar hypoventilation, hypoxemia and secondary polycythemia, these studies are helpful in diagnosis and therapy.

MAURICE G. BUCKLES, M.D.
MOSTAFA DANESHVARI, M.D.
Columbus, Ohio

BIBLIOGRAPHY

Abelmann, H.: Pulmonary Function in Cardiac Diseases. Postgraduate Course, March 1957, Boston, Massachusetts.

Baldwin, E. deF.; Cournand, A., and Richards, D. W. Jr.: Pulmonary Insufficiency: Physiological Classification, Clinical Method of Analysis, Standard Value in Normal Subjects, J. Med. 27:243, 1948.

Comroe, J. H. Jr.; Forster, R. E.; DuBois, A. B.; Briscoe, W. A., and Carlsen, E.: The Lung: Clinical Physiology and Pulmonary Function Test. Chicago: The Yearbook Publishers, Inc., 1955.

Cournand, A., and Richards, D. W.: Physiologic Derangements of the Respiratory System. Clinical Physiology, Grollman-McGraw, Hill Book Company, Inc., 1957.

Curry, J. L., and Ashburn, F. S.: Pulmonary Function Studies in Surgery, Postgrad. Med. 8:220-224, 1950.

Gaensler, E. A., and Maloney, J. V. Jr.: Bronchospirometry, Experimental Observation and Theoretical Considerations of Resistance Breathing, J. Lab. Clin. Med. 39:917-934, 1952.

Gaensler, E. A., and Cugell, D. W.: Bronchospirometry; Ambient Air and Oxygen; Recording Bronchospirometry, J. Lab. Clin. Med. 40:410-430, 1952.

Kovach, J. C.: The Surgeon and Cardiopulmonary Physiology. Dis. of Chest 1:39, 1957.

Lillington, G. A.; Anderson, M. W., and Brandenburg, R. O.: The Cardiorespiratory Syndrome of Obesity, Dis. of Chest 1:1, 1957.

Mead, J.: Principles of Analysis in Respiratory Mechanics. Postgraduate Course in Pulmonary Functions, March 1957, Boston, Massachusetts.

Meneely, G. R.: Pulmonary Function Testing, Dis. of Chest 2:125, 1957.

Motley, H. L.: Clinical Pulmonary Physiology: II. Detection of Early Lung Function Changes in Industrial Exposure, Indust. Med. & Surg. 22:6, 262, 1953. Physiology of Respiration with Reference to Pulmonary Disease, Am. J. Surg. 89, 1955. Pulmonary Function Measurements, ibid. 88:103-116, 1954. The Use of Pulmonary Function Tests for Disability Appraisal, Dis. of Chest 24:378-389, 1953.

Tomashefski, J. F., and Anno, H.: Studies on the Impairment of Respiratory Function in Pulmonary Tuberculosis, Am. Rev. Tuberculosis & Pulmonary Dis. 71:333, 1955.

Tomashefski, J. F., and Atwell, R. J.: Ventilations and Lung Volumes. Clinical Cardiopulmonary Physiology. Grune & Stratton, 1957.

Wright, G. W.: Personal communication.

# New Books

**Books Received.**—The following books have been received by the Editor; they will be reviewed critically as space and facilities permit. Omission of more extended review, however, is not to be taken as criticism of the merit of the book.

**Operative Surgery.** Edited by Charles Rob and Rodney Smith. London: Butterworth & Co., Ltd.; Philadelphia, F. A. Davis Co., 1956. Vols. 1 and 2 of 8 (plus index). Profusely illustrated.

**Proceedings of the Third National Cancer Conference,** Detroit, Michigan, June 4-6, 1956. Sponsored by the American Cancer Society, Inc., and National Cancer Institute, U. S. Public Health Service. Philadelphia: The J. B. Lippincott Company, 1957. Pp. 961.

**Le Diagnostic du Cancer d'Estomac a la Periode Utile (Diagnosis of Carcinoma of the Stomach at the Time Most Favorable for Treatment).** By Rene A. Gutmann. Paris: G. Doin et Cie, 1956. Pp. 257.

**Pathology and Surgery of the Veins of the Lower Limbs.** By Harold Dodd and Frank Cockett. Baltimore: The Williams & Wilkins Company, 1957. Pp. 462, illustrated.

**Spinal Cord Compression.** By I. M. Tarlov. Springfield, Ill.: Charles C Thomas, Publisher, 1957. Pp. 147, with 41 illustrations.

**Men of Medicine.** By Katherine B. Shippen. New York: The Viking Press, 1957. Pp. 220. Illustrated.

**Liver: Structure and Function.** By Hans Popper and Fenton Schaffner. New York, Toronto and London: McGraw-Hill, 1957. Pp. 777. Illustrated. *Reviewed in this issue.*

**Surgery of the Anal Canal and Rectum.** By E. S. R. Hughes. Edinburgh and London: E. & S. Livingstone Ltd., 1957. Pp. 304, with 276 illustrations.

**Halsted of Johns Hopkins.** By Samuel James Crowe. Springfield, Ill.: Charles C Thomas, Publisher, 1957. Pp. 248. Illustrated.

**The Gynecologic Management of Urologic Injuries.** By Henry G. Falk. Philadelphia: F. A. David Company, Publishers, 1957. Pp. 265, with 97 illustrations.

**Perinatal Loss in Modern Obstetrics.** By Robert E. L. Nesbitt Jr. Philadelphia: F. A. Davis Company, Publishers, 1957. Pp. 432, with 108 illustrations.

**The Reticular Formation of the Brain Stem.** By Alf Brodal. Springfield, Ill.: Charles C Thomas, Publisher, 1957. Pp. 87, with 18 illustrations.

**Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus (Movement of the Heart and Blood in Animals: An Anatomic Essay).** By William Harvey. Translated from the original Latin by Kenneth J. Franklin. Springfield, Ill.: Charles C Thomas, Publisher, 1957. Pp. 209. Illustrated.

One of the epoch-making publications in the history of medicine and surgery is here presented, in a handsome little volume whose format, paper and printing indicate due recognition and respect for Harvey's great work. The frontispiece, reproduced by permission of the Royal College of Physicians, is a portrait of the master in full color.

In a translation, the grace, ease and lucidity displayed by Mr. Franklin are nothing short of phenomenal. Harvey's own eagerness, the unmistakable passion for truth that beset him, is vividly conveyed in the opening words of the first chapter: "When . . . I first addressed my mind to seeing how I could discover the function and offices of the heart's movement in animals through the use of my own eyes instead of through books and the writings of others, I kept finding the matter so truly hard and beset with difficulties that I all but thought, with Francastoro, that the heart's movement had been understood by God alone. For I could not rightly distinguish how systole or diastole came about, nor when or where constriction and dilatation occurred. This was because of the rapidity of the movement, which in many animals remained visible but for the wink of an eye or the length of a lightning flash, so that I thought I was seeing now systole from this side and diastole from that side; now the opposite; the movements now diverse, and now inextricably mixed." The reader's own interest and sympathy are instantly aroused, for here is the very romance of all discovery: the fact that what we take entirely for granted today was once a mystery darker than the Catacombs, and one that no human eye had penetrated in all the centuries of the world's history.

This is as it should be. All great discoveries should be presented historically as they were in the beginning, almost literally miracles of human achievement. In reading this limpid translation one seems actually to live and work with Harvey; to watch him as he toils and pauses to ponder; to share with him his moments of discouragement and to share no less those rarer moments when the Truth seems about to break forth upon him.

Mr. Franklin has included also the full original Latin text, a test to which his scholarship is more than equal. The publishers have planned the book, chosen the type and selected the paper, a mellow creamy-white stock, in perfect harmony with the contents. The result is a book that may well be treasured not only by physicians and surgeons but by anyone to whom the great moments of the world's history retain their original beauty and significance.

M. T.

**Mechanisms of Hypertension, with a Consideration of Atherosclerosis.** By Henry Alfred Schroeder. Springfield, Ill.: Charles C Thomas, Publisher, 1957. Pp. 296, with 39 illustrations and 53 tables.

This book is divided into ten chapters of which the eighth and ninth are concerned with the modern treatment of hypertension and an approach to the treatment of atherosclerosis. The tenth chapter is a summary and contains interpretations of what preceded. The initial chapters offer a well-organized explanation of the various mechanisms involved in the production of hypertension, the neurogenic effector mechanisms and the nephrogenic effector mechanisms. Another chapter discusses factors influencing the conversion of neurogenic to nephrogenic hypertension.

There is a most interesting chapter on trace metals and cardiovascular disease. Some of the mechanisms of atherosclerosis are discussed in a chapter, and there is a single chapter which discusses practical modern methods

in the therapy of hypertension. The whole book is well written and is couched in a conversational tone.

In the first paragraph of the preface the statement is made that the purpose of this monograph is to outline the mechanisms aforementioned and to show how changes of these mechanisms indicate specific therapy. In the opinion of this reviewer this chapter might have been extended to cover more exhaustively the therapy of hypertension in general, which would have given the monograph a greater appeal to the clinician.

DAVID GOLDFINGER, M.D.

**Liver: Structure and Function.** By Hans Popper and Fenton Schaffner. New York, Toronto and London: McGraw-Hill, 1957. Pp. 777. Illustrated.

This distinguished offering is the fruit of twenty years' labor in the pathology of the liver by one who was an associate of Eppinger at the University of Vienna. It will be immediately recognized for its wealth of source material and its Herculean digest of the literature, represented by a bibliography of some 4,000 references.

The authors have given the profession a treatise and text on hepatic pathology, but with a special intention. Conceiving of their subject as more than mere description of structure in disease, they have adopted the broader approach of relating structure to function, disease being recognized as malfunction. For this reason they have included a rather extended discussion of normal structure and function, with the result that the book will find use as a sourcebook on many problems of hepatic physiology.

Considering this point of view, the authors have performed a major service in collecting information, presenting current concepts and bringing the material up to date. In all such tasks, of course, there is need for selection, and here the test has been that of practical usefulness to the physician, with a sacrifice of those encyclopedic data and concepts of greater value to the specialist—for example, the experimentalist. It is hoped that a second edition may find room for more of this material if and when the usefulness of this wider scope is indicated.

As to the present wealth of contents, these cover in detail the gross and microscopic structure of the liver, its physiologic and biochemical nature; the clinical, laboratory and pathologic aspects of liver disease; experimental physiology and tests of liver function; hepatic changes in nonhepatic disease; and the correlation of liver tests and biopsies in differential diagnosis.

In addition to its contribution as a review, the book is a record of much new clinical and pathologic material and many original observations by the authors. In a word, a book of first importance, and a valuable addition to the literature of pathology.

M. T.

**The Surgical Management of Pulmonary Tuberculosis.** Edited by John D. Steele. Springfield, Ill.: Charles C Thomas, Publisher, 1957. Pp. 213. Illustrated.

This is the first volume of the John Alexander Monograph Series, published in honor of the great thoracic surgeon whose keen intellect helped him overcome tuberculosis in himself and, despite recurring illness, develop thoracic surgery to a high point. It is appropriate that this, the first in a series that will deal with various phases of thoracic surgery, should present contributions to this specialty on pulmonary tuberculosis.

A number of outstanding contributors have written chapters that might better be described as monographs themselves, each with a generous list of references and each adding dimensions to the treatment of pulmonary tuberculosis, including chemotherapy. The illustrations are excellent. A brief history of the surgical treatment of this disease precedes the chapters on therapy.

Those who contribute, whether as authors or as editors, to works published in honor of some particular great surgeon have one duty above and beyond ordinary responsibilities of publishing: to keep in mind the achievements of the great man aforementioned and set their standards accordingly. Dr. Steele has shown great discrimination in his selection.

M. T.

# Abstracts from Current Literature

**Simple Closure for Perforated Peptic Ulcer.** McCaughan, J. J., and Bowers, R. F., Surgery 42:476, 1957.

Two hundred and seventy-seven perforated peptic ulcers treated over a ten-year period ending Oct. 1, 1956, are here described for the particular purpose of comparing the early and late results of simple closure, with the reported results of emergency subtotal gastric resection for the same disease. Only in recent years have American surgeons undertaken to employ emergency resection for perforated peptic ulcer, although this procedure has been used for many years by European and Russian clinics. It appears that the statistical study and comparison are timely and valuable.

The authors dismiss summarily a third (nonoperative) method for treatment of perforated ulcer by constant gastric drainage, antibiotics and maintenance of fluid balance. This procedure is regarded as less safe than simple closure or plication. The authors utilized the method 11 times. One death resulted when this technic was employed in a case of mistaken diagnosis of acute cholecystitis in a cardiac patient. In the other 10 the patients were hospitalized several days after perforation, with minimal symptoms and signs but with free intraperitoneal air and unquestioned ulcer. This method is used now only when the perforation is adequately sealed to maintain security of the spontaneous closure.

Perforation occurred twice in only 6 patients. There was no instance of a third or fourth perforation.

In the present series only 4 deaths occurred as the result of simple closure or plication. This low mortality rate (1.5 per cent) was achieved in spite of the fact that a great number of patients examined many hours after perforation were elderly or in poor condition otherwise. In support of the authors' preference for simple closure over gastric resection is the observation that in almost all instances of serious postplication complications the patients on admission would have appeared unsuitable candidates for gastric resection as performed by most resectionists today.

Simple closure followed by intensive medical ulcer management provides the possibility of saving the patient's stomach for a number of years. Sixty per cent of 159 patients followed for an average of four and four-tenths years were satisfactorily controlled by medical management. Invalidism is not permitted, and the authors estimate that subsequent definitive surgical treatment of the chronic ulcer will be necessary in about 50 to 55 per cent of the cases (a figure approximately 15 per cent lower than that reported by others). Because of this necessity, the authors support their conservative approach to the acute perforation with the following statements:

1. It is almost a certainty that the widespread use of resection cannot be accomplished with the currently reported mortality and morbidity rates. 2. Subtotal gastric resection has not proved as successful in the permanent control of peptic ulcer as had been hoped. The resectionists admit that approximately 15 per cent of patients remain "gastric cripples." The best results have been reported in series of cases in which the selection for operation has been most carefully considered; poor permanent results have been encountered, particularly in patients below the age of 35. Such selection is of course impossible for the average patient with perforated ulcer, who is "pulled from the street" for this operation.

Prolonged experience has indicated to the authors that many patients, particularly the young, with important psychosomatic difficulties are better handled by prolonged medical care until they are convinced that surgical operation offers the only means of deliverance from chronic invalidism. The all-im-

portant cooperation and understanding so secured will aid greatly in obtaining a successful outcome. Finally, many patients treated by the simple closure-plication operation will live for many happy years before surgical intervention is needed for control. In the opinion of the authors, this period of comparative gastric tranquillity is enormously worthwhile. Distressing postgastrectomy difficulties, such as the dumping syndrome, great loss of weight, diarrhea, weakness and gastric distress, are distinctly more common in patients who are poorly selected and improperly operated upon.

The authors conclude their presentation with the statement that resection at the time of acute perforation is certainly feasible if the ulcer is gastric and if the presence of carcinoma is suspected or proved by biopsy. In the present series there were 41 gastric ulcers, of which only three were malignant. One of the 41 patients was subjected to total gastric resection three weeks after simple closure-plication of his acute perforation and lived for seven years.

THOMAS WILENSKY, M.D.

**The Classification and Principles of Treatment of Gastric Ulcers.** Johnson, H., and Camb, M. B., Lancet 2:518, 1957 (Authors' Summary).

Reasons are given for considering that gastric ulcers should be divided into three separate types having different prognoses and requiring different methods of treatment.

Type I is the commonest and is associated with hyposecretion. It responds to recumbency, but its healing is not accelerated by alkalis. Operation, if it becomes necessary, may be relatively conservative.

Type II is the gastric ulcer that complicates a duodenal ulcer. It is associated with acid hypersecretion and gastric retention. This ulcer has a bad prognosis. It is resistant to medical treatment, tends to become very large and is likely to bleed profusely. Operation is usually required and should be adequate to control the hypersecretion.

Type III is the prepyloric ulcer, which is more like a duodenal ulcer than an ulcer elsewhere in the stomach, and requires similar treatment. It is also more apt to be associated with urgent complications than is an ulcer of Type I.

Reasons are given for the opinion that patients with ulcers of Type I may differ genetically from those ulcers of Type II or Type III.

Principles of treatment are considered in the light of these observations.

HENRY J. ROSEVEAR, M.D.

**The Management of Anastomotic Ulcer.** Balint, J. A.; Cooper, G. W., and Price, E. C. V., Lancet 2:551, 1957.

The authors analyzed the results of treatment of 160 patients with anastomotic ulcers at the Central Middlesex Hospital, the County Hospital, York, and St. James' Hospital, Balham.

The radiologic diagnosis of anastomotic ulceration is difficult, only about 50 per cent being demonstrated by this method. Anastomotic ulcers occurred about ten times as frequently in men as in women, the average age of the patients being 46.

Medical treatment appeared to have little value.

The mortality rate among patients with anastomotic ulcer is high. Fifteen of the authors' patients died of causes related to the ulcer itself or to its surgical treatment.

The authors concluded that partial gastrectomy is the treatment of choice for anastomotic ulcers after gastroenterostomy, especially when this operation is combined with vagotomy.

For anastomotic ulcer following partial gastrectomy, abdominal vagotomy, with or without revision of the anastomosis, or, if necessary, a limited gastric resection to remove the ulcer, is recommended.

For patients with persistently recurring anastomotic ulcers, total gastrectomy will sooner or later be necessary and should not be delayed if anastomotic ulceration recurs after adequate vagotomy and gastrectomy.

HENRY J. ROSEVEAR, M.D.

**Cloth Tubes for Bridging Experimental Abdominal Aortic Defects.** Gotham, B., and Senning, A., Acta Chir. Scandinavica 3:85, 1956.

Tubes of orlon or nylon were used to bridge experimental defects in the abdominal aorta in a series of 12 dogs. The material used was either orlon cloth or nylon cloth; in both cases the warp count was 50 per cm. and the thickness of the thread 0.2 mm. The cloth was folded along the direction of the strands and stitched longitudinally with fine nylon thread, 25 stitches per inch, to make tubes 4.5 cm. in length. The tubes were washed with ether and sterilized by boiling for fifteen minutes. The technic of implantation of the tubes was simple over-and-over suture with No. 5 silk. After resection of the aortic segment, penicillin powder was placed about the suture lines, but heparinization was not employed. The dogs were then observed for periods ranging from two hours to two hundred eighty days. In six of the 12 dogs the tube was totally occluded by thrombosis, and in 2 of these cases late rupture of the suture line occurred. The author concluded that the results are much less favorable with orlon or nylon prosthesis than with aortic homografts.

J. RICHARD MOORE, M.D.

**The Pathogenesis of Peptic Ulcers.** Johnson, H. D., Lancet 2:515, 1957.

Peptic ulcers most often develop in areas that are the sites of local hyperacidity. Patients with duodenal ulcers secrete, on the average, a greater volume of gastric juice and more hydrochloric acid than do healthy persons. This is true both of acid produced in response to stimuli and of acid spontaneously secreted between digestive periods. Samples withdrawn from the duodenal bulb of such a patient is more often acid than is a similar sample taken from a healthy person. In these instances, either insufficient alkali is being secreted or there is a mechanical failure of regurgitation from the second into the first portion of the duodenum. The duodenal defenses are inferior to those of the stomach, for in most patients with duodenal ulcers the stomach resists digestion.

The parietal cells of the stomach secrete acid of 0.159 N in everyone, and the acidity of the gastric juice aspirated depends upon the proportions of its various constituents—alkaline juices from the antrum, gastric mucus, swallowed saliva, and sometimes bile, pancreatic juice and succus entericus regurgitated from the small bowel. Gastric ulcers are most likely to develop in a long hypotonic stomach drawn into a narrow waist at the center.

With the patient in an upright position, the acid parietal juice trickles down the walls of the stomach into the lower portion, or "sump." The walls of the upper portion of the stomach are thus bathed in a mixture of acid parietal juice mixed only with mucus and lacking the alkaline antral juice.

When the patient lies down, the innocuous contents of the sump, including the alkaline antral juice, can wash up over the ulcer; this would explain the relief of pain so commonly experienced by patients with gastric ulcer when they lie down. It has been shown that, of all the therapeutic measures tested, only rest in bed has any statistically significant effect on the rate of healing of gastric ulcers.

The mucous membranes of the stomach are covered by thin layers of secreted mucus. The protective properties of this material are remarkable, as it can neutralize about fifteen times its own mass of N/10 hydrochloric acid. Strong acid penetrates gastric mucus at the rate of about 1 mm. an hour. Normally, mucus is secreted and replaced faster than it is penetrated. Apparently anything that slows down the secretion of mucus at a point where penetration of the mucosa by acid becomes possible would initiate ulceration.

Relative anoxia slows the secretion of mucus, and it is not impossible that it is such slowing, occurring locally, which on occasion allows penetration of the mucus by acid, thus initiating a gastric ulcer.

A possible link between gastric ulcers, arterial-venous shunts and the secretion of epinephrine is hinted at.

HENRY J. ROSEVEAR, M.D.

## IMPORTANT ANNOUNCEMENT

**Contributors of scientific articles for publication in The Journal of the International College of Surgeons from Europe, the Near East and the Middle East should send their articles to:**

**European Office of the**
**International College of Surgeons**
**6-8 Rue de la Confederation**
**Geneva, Switzerland**

**A special committee has been appointed to evaluate the papers submitted for publication. The Journal publishes summaries in English, French, German, Spanish, Italian and Portuguese. Summaries of articles should be included in as many of these languages as possible.**

## AVIS IMPORTANT

**Les auteurs d'articles scientifiques destinés à être publiés dans le Journal du Collège international de chirurgiens sont priés d'adresser leurs articles à l'adresse suivante pour l'Europe, le Proche et le Moyen Orient.**

**Bureau Européen du**
**Collège international de chirurgiens**
**6-8 rue de la Confédération**
**Genéve (Suisse)**

**Un comité a été nommé pour l'examen des articles à paraître. Les auteurs sont priés de joindre à leur travail de brefs résumés en français, anglais, allemand, espagnol, italien et portugais si possible.**

COLLEGE INTERNATIONAL DE CHIRURGIENS
GENEVE 35
FOUNDED BY DR. MAX THOREK

# The Journal of the International College of Surgeons

Official monthly publication of the International College of Surgeons
FOUNDED BY DR. ANDRE CROTTI

**Editor-in-Chief**
MAX THOREK, M.D., ScD., LL.D., F.B.C.S., F.I.C.S., F.P.C.S. (Hon.), F.R.S.M.

**Associate Editor**
PHILIP THOREK, M.D., F.A.C.S., F.I.C.S.

**Consulting Editor**
MORRIS FISHBEIN, M.D., F.I.C.S. (Hon.)

**Assistant Editors**
DOROTHY LANGLEY
HELEN WEISS

**Specialty Editors**

*Cardiovascular Surgery*
Bert Hollis Cotton, M.D., F.I.C.S., D.A.B.
Los Angeles, California

*Genitourinary Surgery*
Michael K. O'Heeron, M.D., F.A.C.S., F.I.C.S.
Houston, Texas

*Neurologic Surgery*
James W. Watts, M.D., F.A.C.S., F.I.C.S.
Washington, D. C.

*Obstetric and Gynecologic Surgery*
J. P. Greenhill, M.D., F.A.C.S., F.I.C.S.
Chicago, Illinois

*Occupational Surgery*
Chester C. Guy, M.D., F.A.C.S., F.I.C.S.
Chicago, Illinois

*Ophthalmologic Surgery*
Paul C. Craig, M.D., F.A.C.S., F.I.C.S.
Reading, Pennsylvania

*Orthopedic Surgery*
Edward L. Compere, M.D., F.A.C.S., F.I.C.S.
Chicago, Illinois

*Otolaryngologic Surgery*
Francis L. Lederer, M.D., F.A.C.S., F.I.C.S.
Chicago, Illinois

*Plastic and Reconstructive Surgery*
Neal Owens, M.D., F.A.C.S., F.I.C.S.
New Orleans, Louisiana

*Proctologic Surgery*
Harry E. Bacon, M.D., F.A.C.S., F.I.C.S.
Philadelphia, Pennsylvania

*Surgery of Thyroid, Parathyroids and Thymus*
Arnold S. Jackson, M.D., F.A.C.S., F.I.C.S.
Madison, Wisconsin

*Thoracic Surgery*
Thomas J. Kinsella, M.D., F.A.C.S., F.I.C.S.
Minneapolis, Minnesota

*Allied Sciences*
Paul Bernard Szanto, M.D., F.A.C.P., F.I.C.S., Chicago, Illinois

Official Journal of the International College of Surgeons, Published Monthly
PUBLICATION OFFICE: 1516 Lake Shore Drive, Chicago 10, Ill.
Entered as second class matter at the post office at Chicago, Ill. under the act of March 3, 1879
Yearly Subscription: Domestic and Foreign, $14.50
Copyright 1958, by the International College of Surgeons

COLLEGE INTERNATIONAL DE CHIRURGIENS
GENEVE 35
FOUNDED BY DR. MAX THOREK

# The Journal of the International College of Surgeons

Official monthly publication of the International College of Surgeons
Edited by Max Thorek, M.D., Sc.D., LL.D., F.B.C.S., F.I.C.S., D.C.M.

EDITORIAL BOARD

Lyon H. Appleby, M.D., C.M., L.R.C.P., F.R.C.S. (Eng.), F.R.C.S. (Can.), F.A.C.S., F.I.C.S.
Vancouver, B. C., Canada

Harry E. Bacon, M.D., F.A.C.S., F.I.C.S., F.R.S.M.
Philadelphia, Pennsylvania

Hamilton Bailey, M.D., F.R.C.S., F.I.C.S. (Hon.)
London, England

Raffaele Bastianelli, M.D., F.I.C.S. (Hon.)
Rome, Italy

Ruston N. Cooper, M.S., F.R.C.S. (Eng.), F.R.C.P. (Eng.), F.I.C.S.
Bombay, India

Paul C. Craig, M.D., F.A.C.S., F.I.C.S.
Reading, Pennsylvania

André Crotti, M.D., F.A.C.S., F.I.C.S.
Columbus, Ohio

Ulysses G. Dailey, M.D., F.A.C.S., F.I.C.S.
Chicago, Illinois

Raymond Darget, M.D., F.I.C.S.
Bordeaux, France

A. Mario Dogliotti, M.D., F.I.C.S. (Hon.)
Torino, Italy

Francisco Graña, M.D., F.A.C.S., F.I.C.S.
Lima, Peru

Gordon Heyd, M.D., F.A.C.S., F.I.C.S. (Hon.)
New York

Claude J. Hunt, M.D., F.A.C.S., F.I.C.S.
Kansas City, Missouri

Oscar Ivanissevich, M.D., F.I.C.S. (Hon.)
Buenos Aires, Argentina

Arnold Jackson, M.D., F.A.C.S., F.I.C.S.
Madison, Wisconsin

Chevalier L. Jackson, M.D., F.A.C.S., F.I.C.S.
Philadelphia, Pennsylvania

Albert Jentzer, M.D., F.I.C.S.
Geneva, Switzerland

William Carpenter MacCarty, Sr., M.D., F.A.C.P., F.I.C.S. (Hon.)
Rochester, Minnesota

Felix Mandl, M.D., F.I.C.S. (Hon.)
Vienna, Austria

Manuel A. Manzanilla, M.D., F.I.C.S. (Hon.)
Mexico City, Mexico

Vasant P. Mehta, M.D., M.S., F.C.P.S., F.I.C.S.
Bombay, India

Henry W. Meyerding, M.D., F.A.C.S., F.I.C.S.
Rochester, Minnesota

Rudolph Nissen, M.D., F.I.C.S. (Hon.)
Basel, Switzerland

Leslie Oliver, M.B., F.R.C.S. (Eng.), F.I.C.S.
London, England

Raffaele Paolucci, M.D., F.I.C.S. (Hon.)
Rome, Italy

Curtice Rosser, M.D., F.A.C.S., F.I.C.S.
Dallas, Texas

Robert L. Sanders, M.D., F.A.C.S., F.I.C.S. (Hon.)
Nashville, Tennessee

Henry M. Scheer, M.D., F.A.C.S., F.I.C.S.
New York City, New York

Jorge Taiana, M.D., F.I.C.S.
Buenos Aires, Argentina

Philip Thorek, M.D., F.A.C.S., F.I.C.S.
Chicago, Illinois

Stephen A. Zieman, M.D., F.A.C.S., F.I.C.S.
Abstract Editor
Mobile, Alabama

PUBLICATIONS COMMITTEE

Francisco Graña, M.D., Chairman
Rudolph Nissen, M.D.
Henry W. Meyerding, M.D.

Max Thorek, M.D., Editor-in-Chief
Arnold S. Jackson, M.D.
Edward L. Compere, M.D.

SUMMARY EDITORS

Dr. Manuel de Cardenas
San Sebastian, Spain
Spanish

Dr. Alipio Pernet
Sao Paulo, Brazil

Dr. José C. Ross
Brazil
Portuguese

Dr. Antonello Franchini and Dr. Martin Mini,
Bologna, Italy
Italian

M. Edwin Fawer
Geneva, Switzerland
French

Dr. Fritz Rothbart, Chicago, Illinois
German

Leslie C. Oliver, F.R.C.S., F.I.C.S.
London